BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

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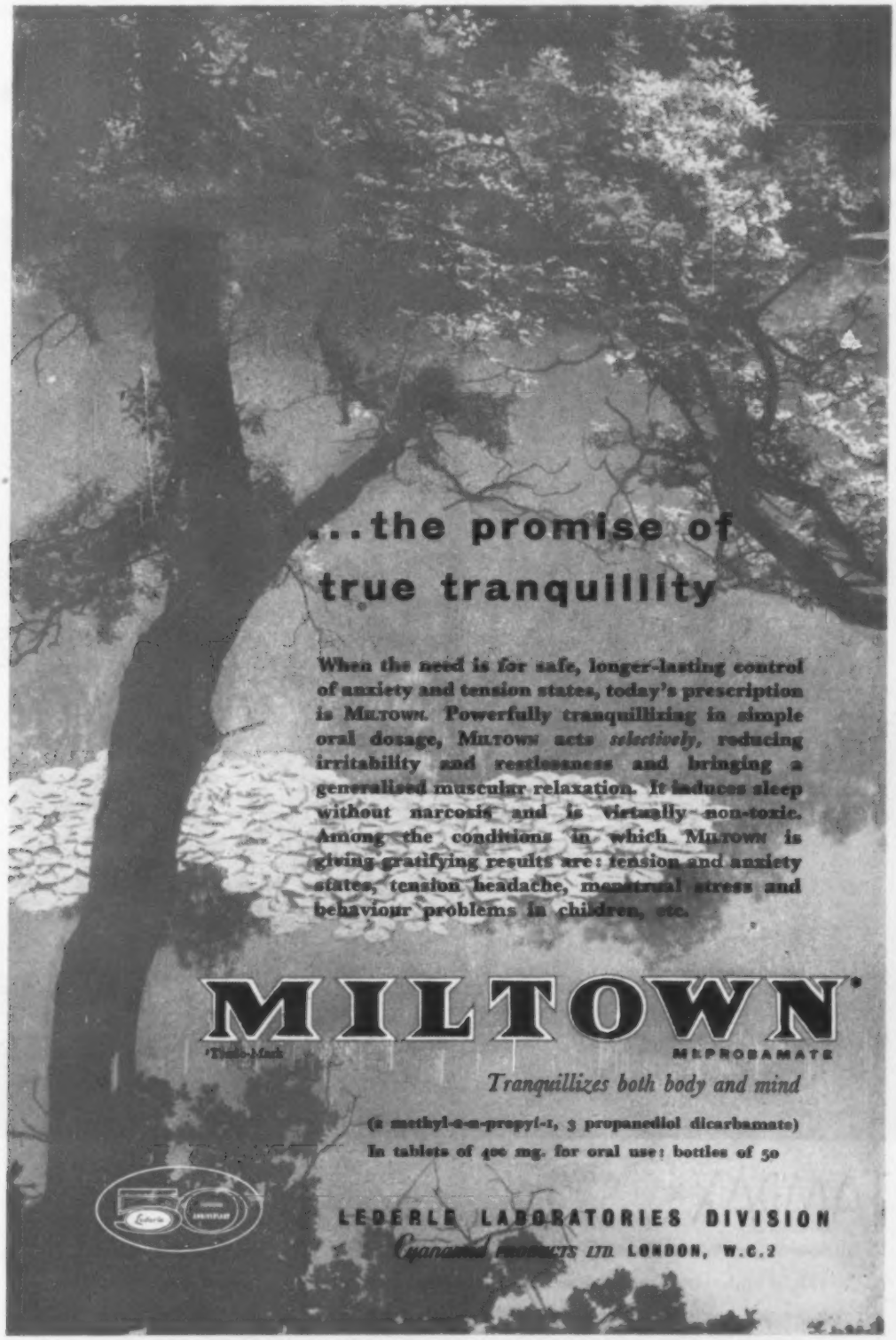
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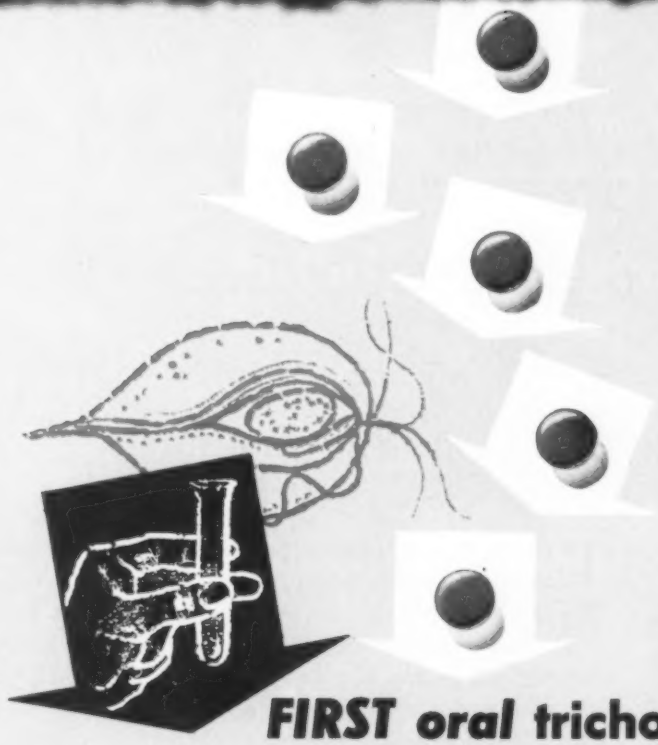

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HYPOGLYCAEMIC AND ANTIDIABETIC SULPHONAMIDES

BY

F. G. YOUNG, D.Sc., F.R.S.

Professor of Biochemistry, University of Cambridge

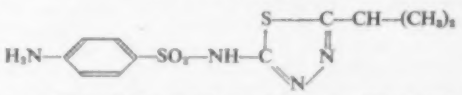
In 1942 Janbon and his colleagues at Montpellier, in the course of treating typhoid fever patients with *p*-aminobenzenesulphonamido*iso*propylthiodiazole (=I.P.T.D., 2254RP, P.A.S.I.T., see formula I), observed that hypoglycaemia sometimes developed and that this could be fatal under the dietary conditions obtaining in France at that time. Professor Auguste Loubatières was able to follow up these interesting chemical observations by laboratory experiments at Montpellier despite the difficult conditions which then prevailed. He has recently summarized his findings concerning the action of I.P.T.D. (Loubatières, 1955). He finds that the administration of the drug by oral or by intravenous means can induce substantial hypoglycaemia in numerous species of animal under conditions of fasting, and in a dog from which the pituitary gland, or the adrenal glands, or the thyroid plus parathyroid glands, together with the gonads, have been removed. Nevertheless, he states that complete removal of the pancreas prevents the hypoglycaemic action of I.P.T.D., although the drug is capable of augmenting the utilization of glucose in the partially depancreatized dog. In the alloxan-diabetic rabbit the daily administration of I.P.T.D. was found by Loubatières to reduce or abolish the diabetic symptoms. Similar but less striking and consistent results were seen in the alloxan-diabetic dog. No evidence was found that the drug could oppose the diabetogenic action in the dog of a crude extract of anterior pituitary tissue.

Cross-circulation experiments with a donor dog treated with the drug, and an alloxan-diabetic recipient animal, led Loubatières to deduce that I.P.T.D. stimulates the secretion of insulin by the β-cells of the pancreatic islets. On the basis of these and other experiments he concludes that the drug may have a dual action on the islets—that of stimulating the secretion of insulin by β-cells and depressing the secretion of glucagon by the α-cells.

In 1952 Davis made the interesting observation that the administration of "synthalin" (decamethylenediguanidine, see formula II) induces degenerative changes in the α-cells of the pancreatic islets of the normal rabbit. This substance was developed many years ago as a synthetic hypoglycaemic and antidiabetic agent, active by mouth (Frank, 1927), and when von Holt and his colleagues at Hamburg (1954, 1955) found that I.P.T.D. also exerts a toxic action on the α-cells of the pancreatic islets it seemed possible that the effects of these two substances might be related. von Holt has in fact ascribed the hypoglycaemic action of I.P.T.D. to its destructive action on the α-cells of the pancreatic islets. (For recent reviews see Ferner, 1956; von Holt *et al.*, 1956.)

Mechanism of Action

On October 7, 1955, a series of publications appeared in the *Deutsche medizinische Wochenschrift* (Franke and Fuchs, 1955; Achelis and Hardebeck, 1955; Bertram



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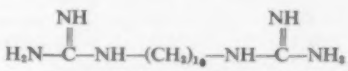
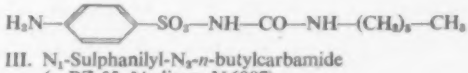


II. Decamethylenediguanidine (synthalin)



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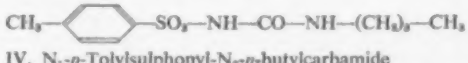

IV. N_1-*p*-Tolylsulphonyl-N_3-*n*-butylcarbamide (=D 860, U 2043, Orinase)

et al., 1955) describing the hypoglycaemic and antidiabetic action of N_1-suphanilyl-N_3-*n*-butylcarbamide (N-butyl-N'-sulphanilylurea, BZ 55, "nadisan," U 6987, see formula III), the substance being active when administered by mouth or parenterally. Apparently, as with I.P.T.D., this sulphonamide derivative was found to possess an important effect on carbohydrate metabolism as the result of chance clinical observation. The first suggestion about the mechanism of its action was that it might inhibit the activity of the α-cells of the pancreatic islets, in line with the views of von Holt and Ferner about the action of I.P.T.D. Subsequently Mirsky and his colleagues (1956) found that BZ 55 and related substances are non-competitive inhibitors of the enzyme found in the liver which destroys insulin (insulinase), and that a diminution in insulinase activity is associated with the hypoglycaemia induced by these substances. The natural suggestion was therefore made that these substances act on carbohydrate metabolism,

at least in part, by preventing destruction of insulin. The fact that these drugs were capable of controlling the symptoms of diabetes in a proportion of patients suffering from this disease might indicate that in some diabetic patients abnormally vigorous destruction of insulin could be a significant factor in the maintenance of the condition (Mirsky *et al.*, 1956).

In addition to its action on insulin BZ 55, like I.P.T.D., appears to stimulate the secretion of insulin by the β-cells of the pancreatic islets (Kracht and Rausch-Stroomann, 1956).

Animal Experiments

In our own laboratory we have given BZ 55 orally to a cat with a diabetic condition which had persisted for about a year after a short period of treatment with growth hormone (metahypophysial diabetes). In the cat, untreated metahypophysial diabetes usually shows spontaneous remission after six to twelve months (Young, 1948), but in this particular animal (No. 286) the diabetes had become mild (5–10 g. of glucose excreted daily) with no sign of complete remission over a period of many months. After two daily oral doses of 20 mg. of BZ 55 the diabetic condition disappeared, and during the following ten days the blood sugar averaged about 50 mg. per 100 ml., as compared with 250 mg. per 100 ml. before treatment with the BZ 55. The animal was killed ten days after the diabetic condition had disappeared, and histological examination of the islets kindly carried out by Mr. K. C. Richardson showed extensive hydropic changes in both α- and β-cells of all the pancreatic islets examined. In cats which show spontaneous recovery from metahypophysial diabetes the α-cells are usually normal in appearance while the β-cells are intensely hydropic (Young, 1948).

Among the chemical relatives of BZ 55 that have been shown to be hypoglycaemic and antidiabetic, the most highly active appears to be N_1-*p*-tolylsulphonyl-N_2-*n*-butylcarbamide (D 860, U 2043, "orinase," see formula IV). This substance is not an obviously active antibacterial agent.

It is of interest to recall that for long it has been known that acridine derivatives possess hypoglycaemic activity (Nielsen, 1929; Monasterio, 1931), while more recently Mendes-Alves (1952) and Mendes-Alves and Gomes (1954) have demonstrated an antidiabetic action of penicillin in partially depancreatized dogs and in alloxan-diabetic rats. The studies of Mendes-Alves were undertaken as the result of the observation that the administration of penicillin to certain diabetic patients induced an alleviation of the diabetic condition, which could not obviously be attributed to the suppression of an infective state. In some instances the amelioration of the diabetic condition persisted after cessation of the treatment with penicillin, and the possibility of an action of penicillin on the cells which produce insulin was suspected (Mendes-Alves and Gomes, 1954).

When one considers the range of substances which exert some degree of hypoglycaemic and antidiabetic action—guanidine derivatives, acridines, sulphonamides, and penicillin—one is struck by the fact that all possess some antimicrobial action. Can these two actions reasonably be related?

At this point I should like to recall the fact that Markowitz, Rappaport, and Scott (see Markowitz and Rappaport, 1951) observed that, although dogs usually die if the hepatic artery is ligated, they survive the operation when given large amounts of penicillin to facilitate postoperative recovery. This unexpected finding led Markowitz and Rappaport (1951) to survey the literature concerning the bacteriology of normal liver. It appears from this that the livers of many species of animal normally contain spore-bearing anaerobic bacteria, and in numerous instances *Cl. welchii* can be isolated. Moreover, tissues of normal animals other than the liver are frequently found to contain bacteria, often anaerobic organisms. But as Markowitz and Rappaport strikingly comment, "It is logical that the liver, situated at the head of the portal system which drains a cesspool, should have bacteria in it more consistently than other tissue." They conclude that penicillin prevents death in the dog, when the hepatic artery is ligated, by inhibiting the growth of anaerobic organisms which otherwise might flourish and produce lethal enzymes such as lecithinase.

Two Pertinent Questions

Although there is evidence that bacteria can lurk in normal tissues and might therefore play a part in the economy of the normal animal, such an idea is foreign to modern thought and is usually ignored. Nevertheless is it not possible that the breakdown of insulin in the normal or in the diabetic animal or patient might result in part from the activity of bacteria present in normal tissues? Is it possible that insulinase might be in part at least of bacterial origin? Certainly proteolytic enzymes are known to be present in many bacteria, including *Cl. welchii*, while the exacerbating effect of infection on clinical diabetes is well recognized. Although no conclusive answer can be given to these questions, the possibility can reasonably be envisaged that the antidiabetic sulphonamides might exert a significant effect by diminishing the number of bacteria, and therefore the amount of proteolytic enzymes, in the tissues, particularly those of the liver. An objection that might at once be raised to this view is that the antidiabetic action and the antibacterial effectiveness of the sulphonamides are not quantitatively related. In particular D 860, which is effective in many diabetic patients, is not obviously antibacterial.

However, when we are dealing with bacteria surviving in normal tissues under presumably special conditions, the question of the accession of the drug to the microbe may well be of paramount importance. A substance with a hydrocarbon non-polar grouping at both ends might have special advantage in this respect and be enabled to bring weak antibacterial action to bear with vigorous effect at the needed site of action. Furthermore, the possibility that the substance which is effective in the tissues is a metabolite of that which we have given to the patient or animal, and not the administered drug itself, should not be ignored in such an instance.

There is evidence that the antidiabetic sulphonamides not only depress the catabolism of insulin but also stimulate the secretion of insulin by the β-cells of the pancreatic islets. Such an action might depend on the stimulation of the secretion of glucagon or other hyperglycaemic substances by the α-cells of the pancreatic islets (cf. Young, 1955), and if such an action occurred the changes in the α-cells observed by some investigators to follow the administration of sulphonamides might be accounted for.

There is at present no simple solution to hand of the problem of the mechanism of action of the antidiabetic sulphonamides. But clearly the observations made in Montpellier in 1942 foreshadowed much that is of growing interest and importance to-day.

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A CLINICAL TRIAL OF BZ 55

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Two groups of German workers have recently reported the successful control of most elderly or middle-aged patients suffering from mild diabetes by BZ 55 (N-butyl-N'-sulphanilylurea) (Franke and Fuchs, 1955; Bertram *et al.*, 1955). It is, however, difficult to assess the therapeutic value of the drug from these reports because the data given are inadequate. When exact figures for diets are stated they seem unduly high by British standards. Certainly many of the patients in whom control was successfully achieved with BZ 55 appeared to have the type of diabetes which would usually have responded to dietary restriction alone, without the use of insulin or an insulin substitute (*British Medical Journal*, 1955).

It was therefore felt that further carefully planned and fully documented clinical trials were necessary to establish the place of these sulphonamide compounds in the management of diabetes.

Selection of Patients

We considered that orally administered BZ 55 would have its main practical use as a complete substitute for parenteral insulin. Since the German work emphasized that such a complete substitution was only rarely possible in the young diabetic, we limited this initial study to patients over the age of 45 suffering from mild diabetes who were not overweight by more than 10% of their ideal weight (Metropolitan Life Insurance Company, Statistical Bureau, 1943, quoted by Dunlop *et al.*, 1953), but who, on a fully restricted diet, continued to show significant hyperglycaemia and glycosuria, and to experience diabetic symptoms in the absence of insulin therapy.

From the diabetic out-patient clinic 65 active patients (5 male, 60 female) who appeared to be of this type were selected and observed as out-patients for periods varying from one to six weeks. None of these patients had any active focus of infection, although many had retinopathy and neuropathy of the diabetic type. Only five were not currently receiving insulin, but they were inadequately controlled by diet alone. Control in those receiving insuiin was good or moderate.

At the first visit each patient was impressed with the necessity of adhering strictly to the diet which they were at that time supposed to be taking, and the administration of insulin was stopped. Thereafter each was seen once or twice weekly, when the blood-glucose concentration was estimated, 24-hour and fasting urine samples were tested for glucose and ketone bodies, and weight and symptoms were recorded.

It was possible to complete the trial of the drug in only 44 of the 65 patients initially selected. Of the 21 patients withdrawn from the trial, either in the out-patient adaptation period or after admission to hospital, seven developed severe ketosis consequent on the withdrawal of insulin, necessitating its further administration. One of these, previously well controlled on 24 units of insulin zinc suspension, was admitted to hospital almost comatose only three days after discontinuing insulin, while another became seriously ketotic on the second day, both of them emphasizing the possible dangers of stopping the administration of insulin even in cases of apparently mild diabetes. Three were rejected because their blood-glucose concentrations four hours after a meal consistently exceeded 480 mg. per 100 ml., and, on the other hand, 10 were discarded when it became clear that adequate control was achieved by dietary restriction alone. In another patient the development of a severe drug fever necessitated the prompt withdrawal of BZ 55 before data were complete.

It can be seen from Tables II and III that all the 44 patients finally included in the analysis required treatment with insulin or an insulin substitute in addition to dietary measures.

Methods

The first 22 patients were studied in hospital for twenty days, and constitute Group I. The remaining 22 patients were in hospital for eight days only, and form Group II.

On admission to hospital all patients were assessed for a control period of seven days in the case of Group I and three days in the case of Group II. BZ 55 was started on the eighth and the fourth day respectively, and the effect of continued dosage was studied for the remainder of the patients' stay in hospital.

The reduction in hospital stay for Group II was made, firstly, because it was clear from experience obtained with Group I that the patients had, with an occasional exception, adhered to their diets during the out-patient adaptation period, so that surprisingly steady levels of hyperglycaemia and glycosuria occurred in the control period in hospital (Figs. 1 to 6); and, secondly, because we were satisfied that the response to therapy could for clinical purposes be accurately assessed by the fifth day of treatment.

The design of the trial was to some extent governed by clinical considerations. Thus, although most factors were kept constant throughout for all patients, the diets were individually prescribed and the dosage of BZ 55 was adjusted according to the clinical response.

Each patient continued to receive the diet which had been taken as an out-patient. The total calculated daily calories, carbohydrate, fat, and protein were kept constant throughout the trial. The same meal each day contained a constant calculated quantity of these proximate principles.

All patients were ambulant, and daily activity was kept as unaltered as possible throughout the trial. Each patient was weighed at the same time daily in the same clothes.

Venous blood was withdrawn by one or other of us each day at 8.30 a.m. (patient fasting), at 4 p.m. (three and a half to four hours after lunch), and at 8.45 p.m. (two hours after the main evening meal). These times were chosen as being best fitted to demonstrate the daily profile and excursion of glycaemia. The specimen taken at 8.45 p.m. reflected the postprandial rise in blood glucose. The blood-glucose content was estimated by one of us (J. D. B.), using the Nelson (1944) modification of the Somogyi method.

24-hour urine collections were obtained daily (8.30 a.m.–8.30 a.m.). The glucose content was estimated by Benedict's quantitative method and nitrogen by the micro-Kjeldahl method by one person.

In the majority of patients, glucose tolerance was measured in the control period either by the standard oral procedure, using a loading dose of 50 g. of glucose (16 patients), or by the intravenous technique (14 patients) (Duncan, 1956). In patients whose response to BZ 55 was satisfactory the test was repeated after five to ten days of

treatment. Due allowance for the glucose given in these tests was made in the daily diet.

Haemoglobin, red blood cell count, white blood cell count, platelet counts, and differential white-cell counts were estimated in the first 22 patients. In the remainder it was possible to estimate only haemoglobin and white blood cell counts. In all, the following tests of liver function were made: plasma albumin and globulin, total serum cholesterol, thymol turbidity, colloidal gold flocculation, and serum bilirubin. Observations were also made on plasma electrolytes, non-protein nitrogen, and CO_2 combining power. In seven patients 24-hour urine A.S.F.S. (acid-stable formaldehydogenic steroids) were determined (Tompsett and Smith, 1954), and in six patients tracer doses of radio-iodine were given for assessment of thyroid activity. All these observations were repeated during treatment with BZ 55.

In the first 12 patients treatment with BZ 55 was started with 3 g. (six tablets) given by mouth before breakfast. In 32 patients the dose was 4.5 g., and in addition blood was withdrawn at hourly intervals for five hours thereafter and its glucose and BZ 55 content were determined. The patient remained in bed and food was withheld during the period of the test. It was hoped that the response to this single dose might be of value in predicting the patient's subsequent response to the continuous administration of BZ 55.

Further dosage was dependent upon the response of the patient. If it was satisfactory, the dose was gradually reduced over three or four days to 1.5 g. (Figs. 2 and 3), but when the response was inadequate it was continued at 4.5 g. daily for several days (Figs. 4 and 5).

The BZ 55 concentration in the blood was estimated by the method of Bratton and Marshall (1939), pure BZ 55 being used for the preparation of standards.

Patients whose response was considered to be clinically satisfactory were discharged on a daily maintenance dose of BZ 55 varying from 1 to 1.5 g. They are being seen

TABLE I.—*Clinical Data of the 44 Patients in Whom the Trial of the Drug was Completed*

	Group I Patients (22)				Group II Patients (22)			
	Responsive (16)		Unresponsive (6)		Responsive (19)		Unresponsive (3)	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
Age at trial (years)	62·4	50–71	62·2	55–74	62·1	45–73	58·2	55–59
,, ,, diagnosis (years)	57·4	44–69	59·0	53–73	54·9	35–67	52·5	43–56
Duration of diabetes (years)	5	0–19	3·2	0–10	7·2	0–18	5·7	2–12
Ideal weight (kg.)	65·4	60–77	69·8	63·5–78	65·3	58–78	64·8	60–73
Weight at trial as percentage of ideal weight	90·2	79–104	85·3	83–95	92·3	76–104	87·2	75–106
Previous daily insulin requirement (units)	18·5	Nil–36	20·3	12–32	21·5	Nil–44	26·7	24–32
Diet: Calories	1,666	1,100–2,400	2,083	1,600–2,400	1,600	1,100–2,400	1,833	1,200–2,200
Diet: Carbohydrate (g.)	131·2	100–200	180·5	140–220	149·5	110–200	160	120–180

TABLE II.—*Group I Patients (22)*

	Responsive and Clinical Successes* (16)		Unresponsive and Clinical Failures* (6)		Responsive and Clinical Successes † (16)	
	Mean	Range	Mean	Range	Mean	Range
F.B.G. Control period	221	142–274	258	171–329	—	—
F.B.G. Treatment ,,	109	71–148	245	158–310	115	67–163
F.B.G. Difference	−112	−71/−157	−13	−30/+25	−106	−63/−158
Av.B.G. Control period	255	187–307	332	258–399	—	—
Av.B.G. Treatment ,,	142	92–185	320	231–366	151	86–198
Av.B.G. Difference	−113	−78/−151	−12	−33/+15	−104	−71/−157
Pp.B.G. Control period	312	220–388	421	304–495	—	—
Pp.B.G. Treatment ,,	204	113–259	406	274–464	214	117–260
Pp.B.G. Difference	−108	−74/−153	−15	−31/+16	−98	−65/−155
Difference F.B.G./Pp.B.G. Control	91	46–136	163	70–212	—	—
Difference F.B.G./Pp.B.G. Treatment	95	42–146	161	70–214	99	48–142
24-hr. urine glucose Control	49·2	22–124	100·8	49–157	—	—
24-hr. urine glucose Treatment	3·5	0–30	96·3	34–153	9·4	0–49
24-hr. urine nitrogen Control	13·7	10·5–17·8	14·9	8·6–19·8	—	—
24-hr. urine nitrogen Treatment	11·6	9·6–15·0	15·0	9·0–21·1	—	—

* Values for treatment period = mean from 5th to 12th day inclusive. † Values for treatment period = mean from third to fifth day inclusive.
F.B.G. = Fasting blood glucose (8.30 a.m. specimen). Av.B.G. = Average daily blood glucose (mean of 8.30 a.m., 4.30 p.m., and 8.45 p.m. specimens.)
Pp.B.G. = Postprandial blood glucose (8.45 p.m. specimen). Blood glucose in mg. 100 ml. Urine glucose and nitrogen in g.

TABLE III.—*Group II Patients (22)*

	Responsive (19)				Unresponsive (3)	
	Clinical Successes (16)		Clinical Failures (3)			
	Mean	Range	Mean	Range	Mean	Range
F.B.G. Control period	203	133–267	309	284–332	273	253–300
F.B.G. Treatment ,,	115	65–149	236	222–245	273	241–300
F.B.G. Difference	−88	−68/−146	−73	−62/−92	0	−12/+13
Av.B.G. Control period	234	190–281	331	324–337	319	302–342
Av.B.G. Treatment ,,	147	89–196	257	253–263	319	297–355
Av.B.G. Difference	−87	−62/−146	−74	−67/−80	0	−17/+13
Pp.B.G. Control period	297	225–362	374	333–401	426	385–448
Pp.B.G. Treatment ,,	215	126–257	299	266–339	429	388–463
Pp.B.G. Difference	−82	−66/−146	−75	−64/−96	+3	−7/+15
Difference F.B.G./Pp.B.G. Control	94	40–160	65	32–117	153	85–191
Difference F.B.G./Pp.B.G. Treatment	100	40–162	63	21–117	156	88–196
24-hr. urine glucose Control	37·8	20·0–76·0	71·8	65·5–76·0	75·3	67–84
24-hr. urine glucose Treatment	5·4	10·0–16·0	34·0	29–41	76·3	69·5–88

Values for treatment period = mean from third to fifth day inclusive. Blood glucose in mg./100 ml. Urine glucose and nitrogen in g.

regularly at intervals of one to two weeks at a special clinic by one or other of us. Each patient is weighed and brings a 24-hour urine collection, the glucose content of which is determined. A sample of blood is withdrawn and estimated for glucose and BZ 55 content, the patient having fasted since breakfast, taken at least four hours previously. Haematological examinations are done at intervals. Initially the patients were instructed to test fasting and evening urine specimens for a few weeks after discharge, but this practice was later discontinued and dummy tablets have been substituted in 12 patients to date. After a period on "dummy therapy," when it became clear that control of the diabetes was deteriorating, they were again given BZ 55. Both substitutions were made without the patients' knowledge. Many, however, were quick to recognize a return of diabetic symptoms while taking dummy tablets.

Comparison of Responsive and Unresponsive Patients

Clinical Features

The clinical data for both groups are presented in Table I. All our patients were over the age of 45 at the time of the trial, and within this middle-aged or elderly group age did not seem to have any bearing on the patient's response to BZ 55. Within the ranges observed in this series, the duration of clinical diabetes, the age of the patient when the diagnosis was made, the daily dose of insulin previously required, and the period of time over which it had been administered were unrelated to the result obtained with BZ 55. The presence of degenerative diabetic changes, or a family history of the disorder, were also without influence upon the result.

The total calorie and carbohydrate content of the daily diet was higher in the unresponsive group. This was due to the fact that on the whole these unresponsive patients were more underweight in relation to their ideal weight than the responsive group.

In seven of the nine unresponsive patients significant ketonuria had previously been recorded. Ketonuria had also been noted in 5 of the 35 responsive patients, but only at the time of diagnosis or in the presence of infection or considerable stress. We formed the strong impression that patients who are prone to develop ketonuria easily do not respond well to BZ 55.

Effect on Hyperglycaemia and Glycosuria

The summarized results for both groups of patients are presented in Tables II and III. From a consideration of the blood-glucose levels and degree of glycosuria found in each patient during the control period it is apparent that all these patients really required insulin. We were impressed by the fact that the level of fasting blood glucose was not a true expression of the impairment of glucose tolerance. Thus, in this series, relatively low fasting blood-glucose levels were combined with poor glucose tolerance, as indicated by a considerable postprandial hyperglycaemia and a relatively heavy glycosuria (Fig. 4). Conversely, high fasting levels were not infrequently associated with a surprisingly good glucose tolerance (Fig. 5; Fig. 6, Case 36). In some of the patients having high blood-glucose values, particularly when the disorder was of long standing, the renal threshold for glucose was elevated so that the small amount of glycosuria present was often misleading (Fig. 2).

Group I

Of the 22 patients in this group, 16 responded favourably to the drug. A fundamental observation on the character of the response was that the amount by which the blood-glucose values were reduced by treatment was virtually the same for each of the three daily determinations for any one patient. Thus there was no appreciable change in the difference between the fasting and postprandial blood-glucose levels before and during treatment (Figs. 1–6). (Mean difference in control period, 91 mg. per 100 ml.—range 46–136 mg.; during treatment, 95 mg. per 100 ml.—range 42–146 mg.) We were therefore unable to confirm the finding of Bertram *et al.* (1955) that the daily profile of glycaemia was narrowed. The mean absolute fall in fasting blood-glucose concentrations for the responsive patients was 112 mg. per 100 ml. (range 71–157 mg.). When the fall is expressed as a percentage of the fasting blood-glucose value, the mean was 50.6% (range 40–61%) (Fig. 8).

In this group all the responsive patients were adequately controlled clinically in that symptoms were abolished, blood-glucose levels were satisfactory, and glycosuria was reduced by at least 75% of the control values. It was considered that adequate control had been achieved when the fasting

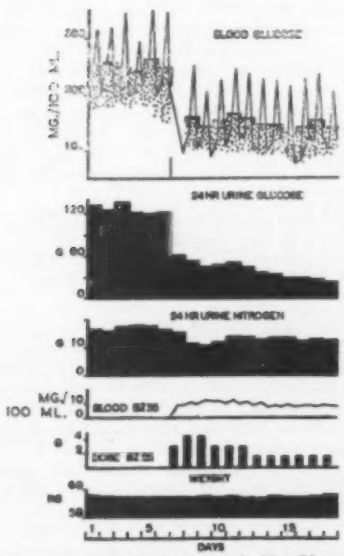

FIG. 1.—Case 2: man aged 64. Note steady values of blood and urinary glucose during control period; immediate response to BZ 55 but no change in daily profile of glycaemia.

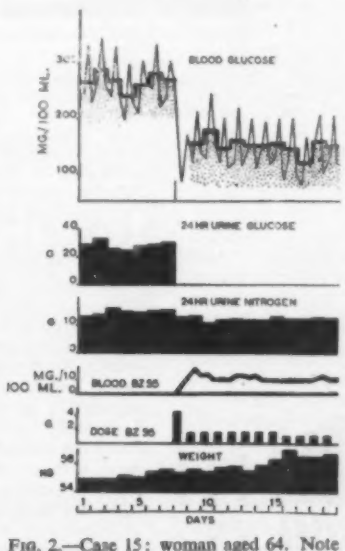

FIG. 2.—Case 15: woman aged 64. Note immediate response to BZ 55; glycosuria completely abolished because of higher renal threshold than Case 2; increase in weight mainly due to full diet not being taken as out-patient.

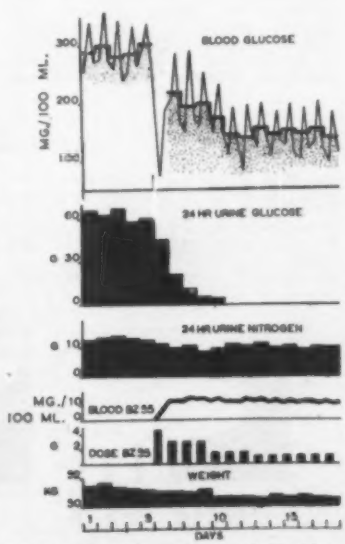

FIG. 3.—Case 20: woman aged 55. Note extreme response to single-dose test causing hypoglycaemia; slower response to continued treatment.

blood-glucose concentration did not exceed 150 mg. per 100 ml., the postprandial value was below 260 mg. per 100 ml., and the average daily blood-glucose level was less than 200 mg. per 100 ml. (Figs. 1–3). It will be seen that the mean values for the group as a whole were much lower than these limits. Some patients who had particularly high blood-glucose concentrations before treatment tended to have a high renal threshold for glucose. Thus glycosuria and symptoms were often abolished with treatment in spite of the persistence in a few cases of relatively high blood-glucose levels. Data for three of the patients successfully controlled by BZ 55 are shown in Figs. 1–3.

Six patients in this group were unresponsive to the drug. The mean absolute fall in their blood-glucose levels was only 13 mg. per 100 ml. (range −33 to +25 mg.). When expressed as a percentage of the fasting blood glucose the mean fall was 5% (−7.5 to +10%) (Fig. 8). All these patients continued to show blood-glucose values exceeding the limits defined for adequate clinical control. Data for two of the patients unresponsive to BZ 55 are shown in Figs. 4 and 5.

In Group I there was no difficulty in assessing the response of any one patient. In all cases it was quite obvious by the fifth day whether or not they were responsive to the drug. Analysis of the response at the fifth day shows that usually it was not significantly less than that at the twelfth day (Table II). The hypoglycaemic effect was therefore rapid and definite (Figs. 1 and 2). The response improved significantly after the fifth day in only three cases, but even in these the absolute fall in fasting blood-glucose levels was greater than 60 mg. per 100 ml. by the fifth day (Fig. 3). This contrasts with the experience of Bertram *et al.* (1955), who found that in 11 of their 28 patients a significant effect was delayed to between the fourth and thirteenth days.

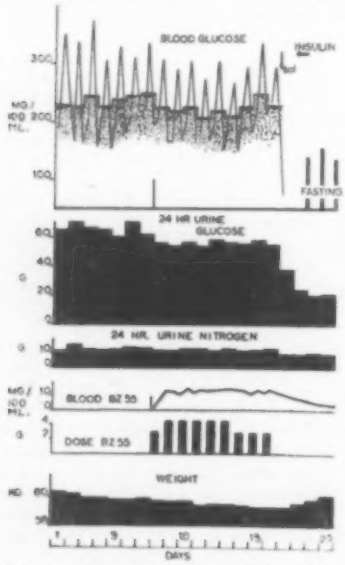

FIG. 4.—Case 12: woman aged 60. Note relatively low fasting glycaemia with marked postprandial hyperglycaemia; lack of response to BZ 55 but sensitivity to insulin; slow fall in blood BZ 55 concentration following cessation of treatment.

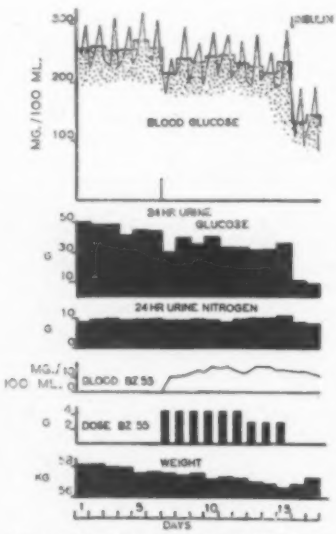

FIG. 5.—Case 8: woman aged 65. Note high fasting glycaemia but small postprandial effect; minimal response to BZ 55 but sensitivity to insulin.

Group II

The effect of BZ 55 on 16 of the 22 patients in this group was of the same character and magnitude as that seen in the responsive patients in Group I. The mean absolute fall in all blood-glucose values was greater than 60 mg. per 100 ml. (range 62–146 mg.). Expressed as a percentage of the control fasting blood-glucose concentration, the mean fall was 43.4% (range 38–55%) (Fig. 8). During treatment each of these patients showed a reduction in glycosuria of at least 75% of the control value, and all of them satisfied our criteria for adequate clinical control.

Three patients showed an absolute reduction in all blood-glucose levels greater than 60 mg. per 100 ml. (mean 74 mg.; range 62–96 mg.). However, their blood-glucose values during the control period were significantly higher than those of the previous 16 patients (Table III). Thus, if the reduction is expressed as a percentage of the control value, it is in all cases less than 30% (mean 23%; range 21–27%) (Fig. 8), and glycosuria was reduced by less than 75% (mean 47%; range 45–54%). These three patients obviously responded to the drug to some extent, but they could not be classed as clinical successes according to our criteria of adequate clinical control, in spite of high dosage with BZ 55. Data for two of these patients are shown in Fig. 6.

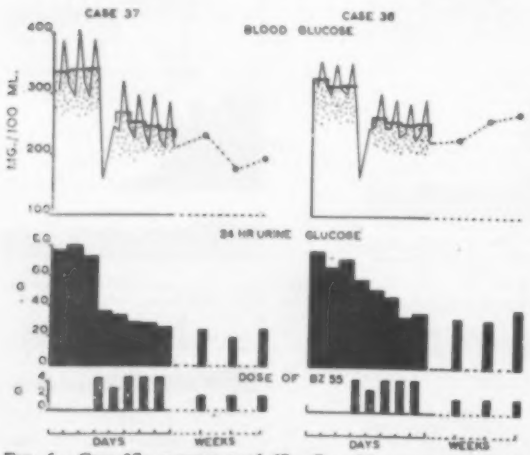

FIG. 6.—Case 37: woman aged 67. Case 36: woman aged 66. In spite of good response to single-dose test and significant response to continued high dosage with BZ 55, neither patient satisfied criteria of successful clinical control.

In three patients the drug was entirely ineffective although again BZ 55 was given in high dosage. The mean rise in their blood-glucose concentration was 1 mg. per 100 ml. (range −17 to +15 mg.) and glycosuria increased by 1 g. daily.

The seven patients who developed ketonuria are not included in this analysis. Four of them were admitted to hospital for the trial. Three developed ketonuria during the control period, and this continued in spite of high dosage with BZ 55, so that insulin had to be administered. When, as a result, hyperglycaemia was less severe and ketonuria absent the patients were subjected to a further trial of BZ 55, again without effect. The remaining patient developed severe ketonuria after five days of treatment with BZ 55, which was therefore replaced by insulin.

Blood-Glucose Values in the Control Period

It can be seen from Tables II and III that both the mean fasting blood-glucose values and the difference between the fasting and postprandial blood-glucose levels of the unresponsive group were considerably higher than those of the

responsive group. There is, however, no clear-cut distinction in this respect between the two groups, hence those values are of little use in predicting response or otherwise in the individual case.

Attempt to Predict Response

Of the 44 patients selected for their probable response, there were 35 who responded to continued dosage with BZ 55, but only 32 of these responded well enough to be classed as clinical successes. Owing to the difficulty of predicting therapeutic success clinically, an attempt was made to obtain this information by the response to the single dose of BZ 55 previously described.

Of the 32 clinical successes, 25 were tested in this way, and in them the mean fall in blood-glucose levels at five hours was 115 mg. per 100 ml. (range 68–185 mg.), and two developed classical symptoms of hypoglycaemia. When expressed as a percentage of the fasting level the mean fall was 53.2% (range 40–73%). The three responsive patients who were not clinical successes had a mean fall in blood-glucose levels at five hours of 148 mg. per 100 ml. (range 123–177 mg.). When expressed as a percentage of the fasting level the mean fall was 47.0% (range 44–51%).

Eight of the nine patients who did not respond to continued dosage with BZ 55 were tested. In this group the mean fall was 78 mg. per 100 ml. (range +1 to 135 mg.). When expressed as a percentage of the fasting blood-glucose level the mean fall was 30% (range 0–47%). Three of them had a fall of over 40%. During this test there was no difference between the blood sulphonamide levels reached by the responsive and unresponsive groups. Thus the value of the test in predicting an individual response is limited to the fact that no patient who showed a fall of less than 35% responded clinically to the drug in continued dosage. A fall of over 40%, on the other hand, did not necessarily mean clinical success. The degree of fall in the acute test was not directly related to that obtained with continuous dosage in any individual case.

Factors Affecting Response

Fasting Blood Glucose.—In responsive patients who were also clinical successes the fall in fasting blood glucose was roughly proportional to the fasting blood-glucose concentration in the control period. In the unresponsive group, however, there was no such relationship. The three responsive patients who were clinical failures occupied an intermediate position (Fig. 7). If the absolute fall is expressed as a percentage of the control fasting blood glucose, the patients group themselves in the same way (Fig. 8).

Difference between Fasting and Postprandial Blood Glucose.—The degree of fall in both groups bears no relation to this value.

Blood Sulphonamide Level.—The dosage of the drug was determined by its clinical effect upon the blood-glucose concentration, and varied widely from patient to patient. In any one patient following a known dose, the concentration of BZ 55 in the blood remained remarkably constant, but in different patients given the same dose considerable variation in the blood levels occurred. The levels produced in both the responsive and unresponsive groups were of the same order, although the latter received much larger quantities of the drug. For each responsive patient there seemed to be a minimal therapeutic blood level which again varied from patient to patient.

Other Observations

Urinary Nitrogen Excretion.—It was not practicable to undertake absolute nitrogen balances in such a number of patients. The daily urinary nitrogen excretion was, however, estimated in 22 patients over 20 days. Since the daily diet was kept constant and the number of observations was large, some significance may be attached to the results. From Table I it can be seen that in the 16 responsive patients in Group I the mean control 24-hour urinary nitrogen was 13.7 g., whereas the mean value from the fifth to the twelfth day of treatment was only 11.6 g. This change is statistically significant ($P=0.005$). In this connexion it may also be of interest to note that in the unresponsive patients there was no change in the urinary nitrogen excretion, the values being 14.9 g. for the control period and 15.0 g. for the period of treatment.

Glucose Tolerance.—Three measurements of glucose tolerance have been employed. (1) The difference between the fasting and postprandial blood-glucose concentration was used as a rough index of glucose tolerance. From Tables II and III it can be seen that there is no appreciable change in this value in the responsive or unresponsive groups as the result of treatment with BZ 55 (Figs. 1–6). (2) Oral glucose-tolerance tests before and during treatment were carried out on 10 of the successfully treated patients. At the time of the test the mean fasting blood glucose in the control period was 247.6 mg. per 100 ml., and during treatment 146.5 mg. per 100 ml. It can be seen from Fig. 9 that BZ 55 was without effect either on glucose tolerance or on the rate of its absorption. (3) Intravenous glucose-tolerance tests before and during treatment were performed on 11 of the successfully treated patients. At the time of the test the mean fasting blood-glucose concentration in the control period was 221.8 mg. per 100 ml., and during treatment 108.5 mg. per 100 ml. The mean increment index (Duncan, 1956) for the control test was 1.46 (S.D. 0.3) and during

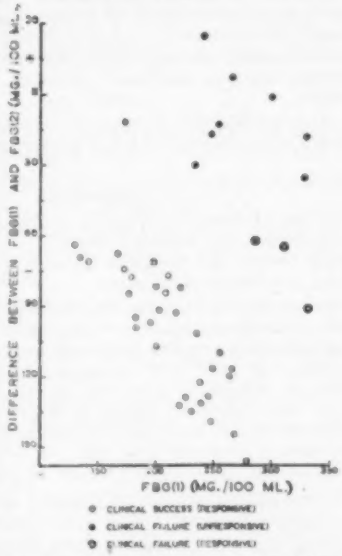

FIG. 7.—Graph relating fasting blood glucose to absolute reduction in fasting blood glucose obtained by treatment with BZ 55. F.B.G. (1) = Mean of values in control period. F.B.G. (2) = Mean of values during treatment.

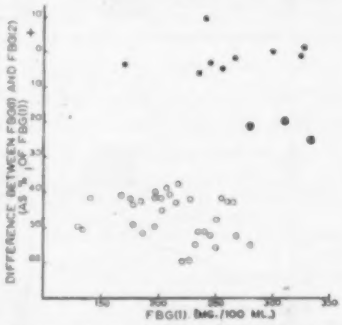

FIG. 8.—Graph relating fasting blood glucose (1) to reduction in F.B.G. obtained by treatment with BZ 55, the reduction being expressed as a percentage of F.B.G. (1). F.B.G. (1) = Mean of values in control period. F.B.G. (2) = Mean of values during treatment. (Symbols as for Fig. 7.)

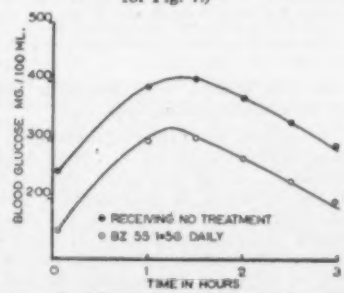

FIG. 9.—Mean of oral glucose-tolerance curves obtained in 10 responsive patients before and during treatment with BZ 55.

treatment 1.45 (S.D. 0.3). It is therefore clear that BZ 55 is without effect on glucose tolerance. We are reporting these observations in detail elsewhere.

Insulin Sensitivity.—We were unable to confirm that "unresponsive patients reacted poorly to insulin" (Franke and Fuchs, 1955). All our unresponsive patients were given a test dose of 20–30 units of soluble insulin in the fasting state, and all showed a profound drop in blood glucose, three becoming clinically hypoglycaemic (Fig. 4). All these patients are now very well controlled on small doses of insulin.

Weight.—While in hospital no very significant changes in weight were observed in the responsive patients.

Side-effects

A few patients complained of mild headache, malaise, and drowsiness when receiving the higher initial doses of the drug. When the dose was reduced to maintenance levels these symptoms disappeared.

In one patient a definite drug fever occurred on the fourth day, necessitating temporary withdrawal of the drug. The hypoglycaemic response had, however, been so good in this patient that after four weeks of out-patient observation, when no insulin was given, the administration of BZ 55 was once again cautiously started in daily doses of 0.5 g. No untoward effects occurred, and control has since been most satisfactory (Fig. 10, Case 45).

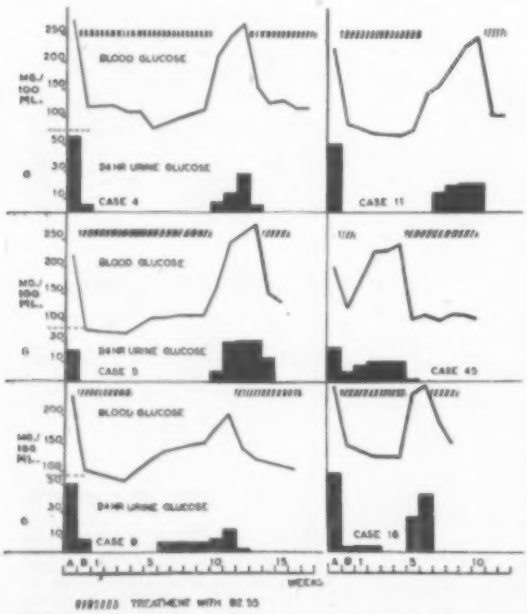

FIG. 10.—Data of six out-patients in whom courses of BZ 55 were interrupted with a return of hyperglycaemia and glycosuria. Values during periods A and B are the mean of those obtained in hospital during the control and treatment periods respectively. The blood-glucose concentrations refer to the fasting values.

In three patients a sulphonamide rash was seen, which, however, spontaneously regressed.

We have so far observed no alteration in the liver-function tests, serum electrolytes, or urinary A.S.F.S. as the result of treatment. There was some depression of iodine uptake by the thyroid in the six patients so tested during the initial two weeks of treatment, which, however, returned to normal during maintenance therapy (Kinsell *et al.*, 1956). One patient, who had for years been receiving 1 gr. (65 mg.) of thyroid daily for myxoedema, became increasingly hypothyroid after two months' treatment with BZ 55, but improved again when the dose of thyroid was doubled.

In the series as a whole there was a definite granulocytopenia in the initial two weeks of treatment. In the majority the count returned to normal despite continuance of BZ 55 in maintenance dosage, but in a few leucopenia has persisted. The lowest white-cell count recorded was 2,000 per c.mm.

A more disturbing feature has been the depression of the blood platelets. One patient reported with spontaneous purpura after only 10 days' treatment with BZ 55, and was found to have a platelet count of 60,000 per c.mm. The count returned to normal and the Hess test became negative within a week of discontinuing treatment. A test dose of 1.5 g. of the drug for two days resulted in a recurrence of thrombocytopenia and a positive Hess test. Another patient then presented with spontaneous purpura, and in this case a leucopenia was also present, the white-cell count being 2,300 per c.mm. This patient is at present being investigated in hospital.

Consequent on this experience platelet counts have been made on 30 out-patients, in none of whom the daily maintenance dose of BZ 55 had exceeded 1.5 g. The technique used was that of Oettle and Spriggs (1951), which gives a normal range of 250,000 to 350,000 per c.mm. Six of these 30 patients have been found to have counts under 180,000 per c.mm., the lowest value being 90,000 per c.mm., associated with strongly positive Hess tests, bringing the total of patients with thrombocytopenia to eight. Three of these had had platelet counts made during the control period before BZ 55 was given, all of which were at the lower limits of normal. Three other patients, although not thrombocytopenic, have shown a substantial fall in platelet counts in comparison with their control figures, and one of these has experienced severe menorrhagia. Among the patients who showed no reduction in platelets, four showed a slightly positive Hess test, a not unusual finding in elderly diabetics, particularly those with retinopathy (Beaser *et al.*, 1944).

Thus the haematological findings so far suggest that BZ 55 has a toxic action on the platelets, and, to a less extent, on the white blood cells. The red cells appear to be unaffected. A more detailed haematological investigation is at present being undertaken and will be fully reported at a later date.

Follow-up

Since discharge from hospital all the clinically responsive patients have been seen regularly. Five have been observed for 18 weeks, 2 for 16, 8 for 10, 4 for 8, 7 for 5, and 6 for 4 weeks. While receiving BZ 55 they have continued to be free of diabetic symptoms and have felt well. Blood-glucose levels and BZ 55 concentration in the blood have remained remarkably steady and satisfactory, and glycosuria has been absent or minimal. A slow but definite increase in weight has been recorded in most patients during this out-patient period of observation. Two patients on a maintenance daily dose of 1 g. of BZ 55 reported symptoms typical of hypoglycaemia which disappeared when dosage was reduced to 0.5 g. daily.

Dummy tablets have been substituted for BZ 55 in 12 patients. In all these the blood-glucose level and glycosuria started to increase within two weeks of stopping the drug, subsequently reaching the levels observed prior to treatment—10 within one month after stopping BZ 55 and 2 by the end of eight weeks. In most cases the hyperglycaemia and glycosuria were associated with a return of diabetic symptoms. The rate at which each of these patients became uncontrolled corresponded to the rate at which their diabetes became uncontrolled after withdrawal of insulin prior to the trial. At this point treatment with BZ 55 was reinstituted and good control was again achieved in all within one week (Fig. 10).

It was notable that an increase or a decrease in glycosuria lagged behind corresponding changes in blood-glucose concentration, which suggests that the drug may have some effect on the renal threshold for glucose. The three patients in Group II who showed a response to BZ 55 but were

classified as clinical failures were continued on 2 g. daily as out-patients and have been observed for three weeks. All three must continue to be classed as clinical failures, though in one there has been some diminution in glycaemia and glycosuria (Fig. 6).

Discussion

There can be no doubt that BZ 55 has a remarkable hypoglycaemic action in some diabetic patients. From our observations this would seem to be due to a reduction in the fasting blood-glucose value. Glucose tolerance is unchanged and there is no alteration in the daily profile of glycaemia, though the absolute values are set at a lower level and glycosuria is reduced or disappears. How this hypoglycaemic action is brought about remains unknown, and this preliminary clinical study was not designed to elucidate this point.

The number of patients likely to benefit from the administration of BZ 55 is limited. The evidence suggests that the drug is of little or no value in the treatment of the young type of diabetic and absolutely contraindicated for those with a marked tendency to develop ketosis. On the other hand, though the mild diabetes of obese patients may well respond satisfactorily to the drug, there should be no substitute for dietetic restriction in the control of such patients. There remains a limited group of middle-aged or elderly non-obese patients suffering from comparatively mild diabetes who, in spite of dietetic treatment, require small or moderate doses of insulin, and for these BZ 55 may provide a welcome alternative. From a group of 55 patients of this type only 33 were adequately controlled by the drug. This is a smaller proportion of successful cases than has been claimed by other workers (Franke and Fuchs, 1955), who, however, may well have used BZ 55 as a substitute for dietary restriction.

When our clinical failures are considered, some are found to have been completely refractory to the drug; in some the response was insignificant; and in a few, although a good response occurred as evidenced by a fall of 60 to 90 mg. per 100 ml. in the blood-glucose concentration, this was insufficient to establish clinical control owing to the very high initial blood-glucose levels. Patients who readily became ketotic proved unsuitable subjects for this treatment. They seldom responded to it, and the drug itself was without effect on diabetic ketosis.

In those patients in whom treatment with BZ 55 resulted in satisfactory clinical control the reduction in glycaemia was of the order of 100 mg. per 100 ml. (range 65–160 mg.). Besides having their blood-glucose levels reduced to satisfactory figures and their glycosuria abolished or greatly reduced, these patients were rendered free from diabetic symptoms. They felt well and put on weight, and there seemed little doubt that some improvement in nitrogen balance occurred. When dummy tablets were substituted for BZ 55 deterioration began to take place within a short space of time, so that in these patients there did not seem to be any place for intermittent treatment, which has been suggested by Franke and Fuchs (1955).

A high incidence of toxic effects was observed in this series—skin reactions, drug fever, slight granulocytopenia, and particularly thrombocytopenia, associated in two cases with spontaneous purpura.

It may well be questioned whether convenience alone justifies the replacement of a well-tried and safe parenteral preparation by an oral substitute in the case of a small percentage of diabetics, especially when its toxic potentialities are considered and when the dangers of its misuse in unsuitable cases are appreciated. Even in patients who might seem to be suitable for such treatment selection is possible only by trial and error, and in those who prove unresponsive ketosis may develop rapidly on withdrawing insulin. Further, in patients who are ordinarily well controlled by BZ 55 an intermittent infection may produce dangerous ketosis which is unaffected by the drug.

BZ 55 will almost certainly prove to be a valuable research weapon which may help to elucidate some of the obscure problems of diabetic metabolism. Nevertheless, we believe that it would be premature at the present time to make it generally available for therapeutic use. This should await the results of further study in special centres to establish the pharmacological action of the drug, to assess its long-term toxicity, and to crystallize more completely the indications and contraindications for its use in any individual patient.

Summary

BZ 55 proved to be an effective substitute for insulin in 33 of 55 middle-aged or elderly diabetic patients.

The drug was without effect on ketosis or on those patients who readily developed ketosis.

The difficulties in selecting the responsive patient and the dangers of withdrawing insulin in the unresponsive patient are emphasized.

The character of the hypoglycaemic response has been analysed with particular reference to the daily profile of glycaemia, glucose tolerance, and its relationship to fasting blood-glucose values.

From follow-up studies it is concluded that maintenance treatment with BZ 55 requires to be continuous and not intermittent.

Minor toxic effects were encountered in several patients, and there appears to be a possibility that thrombocytopenia may occur with alarming frequency.

BZ 55 should not be given as a substitute for dietary restriction. If this principle is observed the number of patients in whom it can replace insulin is more limited than reports to date have suggested.

We are indebted to many people for nursing, dietetic, biochemical, and medical assistance, and particularly to our patients, whose co-operation enabled the study to be undertaken. Our thanks are due to the British Insulin Manufacturers for supplies of BZ 55

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The work of the department of obstetrics in Adeyo Hospital, Nigeria, which serves three-quarters of a million people, is described in the "Clinical Report" of the department of obstetrics, University College, Ibadan, for the period April 1, 1953, to December 31, 1954. The report is by Drs. J. B. Lawson and U. G. Lister and contains 25 tables analysing the work of the department. Ibadan is the largest city in tropical Africa; more than half the population are Mohammedans, and the majority are polygamous. The diet is grossly deficient in proteins needed for a pregnant woman, and anaemia of pregnancy is the most serious complication encountered. The patients themselves are suspicious of scientific medicine; native medicines are often the cause of major disorders. Of a total of 5,985 patients, 5,582 were delivered in hospital. There were 76 maternal deaths (only 3 of which were considered to be not ultimately preventable), 409 stillbirths, and 333 neonatal deaths. The department's facilities were "at an appallingly low level," but a mile away a new hospital has been built where there will soon be 110 obstetric beds.

TRIAL OF AN ORAL HYPOGLYCAEMIC AGENT IN DIABETES

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During an investigation in man of the chemotherapeutic properties of some new sulphonamides, Franke and Fuchs (1955) reported that one, N-butyl-N'-sulphanilylurea (BZ 55), produced hypoglycaemia. Following this observation the compound was examined clinically in diabetics by Franke and Fuchs and by Bertram, Bendfeldt, and Otto (1955). Pharmacological observations were described by Achelis and Hardebeck (1955).

Subsequently, another hypoglycaemic agent, N-(4-methyl-benzosulphonyl)-N'-butyl-urea (D 860) was discovered, on which joint clinical and pharmacological studies were described by Bänder *et al.* (1956). This preparation is not a sulphonamide and has no bacteriostatic activity, but its hypoglycaemic properties are similar to those of BZ 55.

It was evident from German data that these compounds successfully controlled hyperglycaemia and glycosuria in some diabetics, many of whom were overweight. This latter fact suggested to us that in this country some of their successful cases might have been treated by diet alone.

In view of this we decided to undertake a detailed in-patient study on a group of 45 diabetics, from which we attempted to obtain information on the effect of stopping insulin under conditions of constant diet. If hyperglycaemia and glycosuria persisted BZ 55 was administered orally to ascertain its value as a substitute for injected insulin. In addition, information was sought on the possibility of establishing a short-term test which might enable us to predict the usefulness of this drug in long-term therapy.

Studies of free and conjugated sulphonamides in blood and urine were undertaken in an attempt to find correlation between these levels and therapeutic activity.

Methods

Selection of Cases.—Although an attempt was made to get a representative cross-section of the diabetics attending the hospital clinic, numbering just over a thousand, the necessity of spending two weeks in the wards meant a preponderance of middle-aged or elderly female diabetics in those who were admitted. The majority (34) were out-patients already receiving insulin, the need for which had previously been established. Eleven others had not been receiving insulin. Seven of these were newly diagnosed diabetics who would normally have received insulin. Four others have had diabetes for several years, controlled by diet alone; but increasing glycosuria, hyperglycaemia, and loss of weight had latterly suggested their need for insulin. A group of six young and brittle diabetics were admitted for a few days only and took part in a short-term test.

Design of Trial.—On admission each patient was given a diet suitable for his or her physique and metabolic needs, prepared in a diet kitchen. For out-patients of long standing this was a continuation of the diet to which they were accustomed. These diets have been maintained since the patients were discharged. Apart from the group of young diabetics, patients were kept under observation in the wards for at least two weeks, and were then followed up twice weekly in a special out-patient clinic. For the first five days after admission patients were maintained without insulin on diet alone. Once the initial control period had been completed, a two-day test was performed. On these two days no breakfast was given, but on the second day BZ 55, in a dose of 50 mg./kg. body weight, was administered by mouth. This sequence enabled us to assess the effect simply of the omission of breakfast. In a first group of 12 patients, blood and urine sugar and sulphonamides were estimated hourly for six hours, while in subsequent tests samples were obtained every three hours under the same conditions. The patients were kept in hospital and maintained on BZ 55 for at least a further five days. If there was evidence that hyperglycaemia and glycosuria were diminishing, the diabetics were continued to be maintained on BZ 55 as out-patients for at least two weeks. In those who failed to respond even to an increased dosage, insulin therapy was resumed.

Dosage.—The initial dose was 50 mg./kg. body weight for each case—that is, 2.5 to 3.5 g. a patient—and was given in the morning. Except for the young and brittle cases, patients received a dose of 2 g. on the following morning, followed by 1 g. daily for at least five days as in-patients, and then as out-patients. Where control was poor, 3 g. daily was begun on the eighth day and continued for five days. In some, rapid loss of weight and ketosis necessitated an earlier resumption of insulin therapy, which also eventually became necessary in those patients in whom trebling of dose had been attempted.

Body Weight.—Patients were weighed daily; this was continued when they attended as out-patients.

Laboratory Tests.—On admission of patients the following examinations were performed to exclude relevant disease and for later reference: urine tests for albumin and casts; haemoglobin estimation, white-cell count and differential; and serum bilirubin, thymol turbidity, and alkaline phosphatase.

Urine Sugars and Sulphonamides.—Each day 24-hour specimens of urine were collected, the volume was measured, and the total sugar was estimated by Benedict's quantitative method (King, 1951). When BZ 55 was given, the amounts of free and conjugated sulphonamides were estimated by the method of Bratton and Marshall (1939). Urine was also tested four-hourly for sugar and acetone and charted in the usual way.

Blood Sugar and Sulphonamides.—Samples of venous blood were obtained at least three times daily, including a fasting, pre-lunch, and post-lunch specimen, and the sugar was estimated by the method of Hagedorn and Jensen (1923). When BZ 55 was administered the levels of free and conjugated sulphonamides were also estimated by the method of Bratton and Marshall. All estimations were continued on out-patients whenever they attended, bringing with them a 24-hour specimen of urine in a winchester provided.

Results

The patients were divided into two groups, successes and failures, depending upon their response to BZ 55. The blood-sugar levels of those in the successful group fell to within normoglycaemic limits following the administration of the drug, either whilst the patients were in hospital or during the subsequent follow-up as out-patients, and glycosuria almost or completely disappeared during the corresponding period of observation. Within the group of failures

the blood-sugar levels either were not reduced following the administration of BZ 55 or were reduced, but not to within the normoglycaemic range, and the amount of glycosuria was still significant.

Within these two classifications the data were studied statistically under the following headings: (1) Previous history of diabetes. (2) The mean change in blood sugar, glycosuria, volume of urine excreted, body weight, and sulphonamide levels during up to five days in hospital after treatment with BZ 55 compared with the corresponding period in hospital before treatment, during which the patient received no insulin. (3) The two-day test referred to under "Methods," in which the patient received BZ 55 for the first time.

In all the analyses which follow, the maximum amount of data available has been used. For example, it was obviously impossible to continue the administration of BZ 55 to the young and brittle diabetics beyond the first dose in the two-day test because of ketosis and the consequent risk of coma. In such instances the results can be included only when considering data from the two-day test or from previous history of diabetes.

Sex, Present Age, and Duration of Diabetes.—Table I shows the results from 45 cases. An analysis of variance revealed neither regression of age on the duration of diabetes nor any significant difference in the duration of the disease in successes and failures. This is not surprising in view of the wide range of the duration of diabetes within each group. In the successful cases the mean age is slightly higher ($P<0.05$) than in the failures. Since the majority of patients in this study were elderly female diabetics the significance of the age factor would probably have been increased if a larger number of young diabetics could have been included, since none of the young brittle diabetics responded at all to BZ 55.

TABLE I.—*Distribution of Sex, Present Age, and Duration of Diabetes*

Present Age (Years)	Successes (19)		Failures (26)	
	Males (3)	Females (16)	Males (10)	Females (16)
21–40	0	0	4	2
41–60	1	3	3	6
61–80	2	13	3	8
Mean age and range (years)	65 (51 to 77)		55 (22 to 80)	

Duration of Diabetes (Months)	Successes	Failures
0–12	9	6
13–60	6	5
61–120	1	6
121–240	3	7
>240	0	2
Mean duration and range (months)	50 (0 to 192)	104 (0 to 324)

Family History and Complications.—There was evidence of diabetes in the families of 3 out of 16 successful cases and in 3 out of 25 of the failures. The complications are shown in Table II. These data are collected from too small a number of patients for a significant statistical assessment, but there does not appear to be any difference in the distribution of complications between the two groups.

TABLE II.—*Number of Cases Showing Complications*

	Successes	Failures
Retinopathy	4	5
Nephritis	1	1
Claudication	0	2

Insulin Requirements.—Table III shows the mean daily dose of insulin given to patients in both the successful and unsuccessful groups at the time when the present study was started, and the mean change in insulin requirements from the time when the disease was first diagnosed.

TABLE III.—*Correlation Between the Daily Requirements of Insulin Just Prior to the Test with BZ 55 and the Amount of Insulin Required When the Diabetes was First Diagnosed*

	Daily Dose of Insulin Just Prior to the Test with BZ 55		Change* in Daily Dose of Insulin from Time when Diabetes was First Diagnosed until Just Prior to Test with BZ 55		No. of Cases
	Mean (Units)	Range (Units)	Mean (Units)	Range (Units)	
Successes	13·3	0 to 32	−9·8	−54 to +6	16
Failures	40·8	0 „ 120	+10·7	−24 „ +90	25

* −, Decrease in insulin requirements. +, Increase in insulin requirements.

A statistical analysis revealed that the insulin requirements of those patients in the group of failures were significantly greater ($P=0.001$) than the requirements of those in the successful group prior to the administration of BZ 55, and the successful patients needed slightly less insulin at this time and the unsuccessful patients slightly more ($P=0.05$) than they did when the diabetes was first diagnosed.

Present Age, Duration of Diabetes, and Deviation from Ideal Body Weight.—The ideal body weights of 38 patients were determined, using the table of Kemsley (1951–2), and are shown in Table IV. There was no significant difference between the mean deviations in body weight for the two groups, nor was there any correlation between the deviation from ideal body weight and the duration of diabetes or present age when the data in Table I were analysed with those of Table IV.

TABLE IV.—*Deviation of Actual Body Weight from the Ideal Body Weight*

	Deviation* from Ideal Body Weight (lb. and kg.)		No. of Cases
	Mean	Range	
Successes	−3 (−1·36 kg.)	−44 to +42 (−19·96 to +19·05 kg.)	15
Failures	−11 (−4·99 kg.)	−46 to +16 (−20·86 to +7·26 kg.)	23

* −, Underweight. +, Overweight.

Deviation from Ideal Body Weight Before Administration of BZ 55 and the Change in Body Weight Whilst in Hospital following its Administration.—One possible action of BZ 55, if it restores a normal metabolism, would be its effect on the body weight of the patient where an obese patient might be expected to show a decrease in weight and a thin patient an increase. The data from 37 cases were available in which daily observations on body weight were made carefully in the period before and after the administration of BZ 55 while the patients were in hospital. Table V shows the results obtained. There was no correlation between the change in body weight after BZ 55 and the deviation from the ideal body weight for either group, nor was there any significant difference between the two groups in either change in body weight or deviation from ideal weight. The lack of significance, however, could be due to too small a

TABLE V.—*Deviation from Ideal Body Weight Prior to BZ 55 Administration and Change in Body Weight Following its Administration*

		Deviation from Ideal Body Weight lb. (kg.)	Change in Body Weight oz. (g.)	No. of Cases.
Successes	Mean	−3 (−1·36 kg.)	−14 (−397 g.)	13
	Range	−44 to +42 (−19·96 to +19·05 kg.)	−13 to +54 (−368 to +1,531 g.)	
Failures	Mean	−16 (7·26 kg.)	−7 (−198 g.)	12
	Range	−49 to +16 (−22·25 to +7·26 kg.)	−88 to +44 (−2,495 to +1,247 g.)	

number of cases or too short a period of observation of body weight after BZ 55.

Effect of BZ 55 on Fasting (6 a.m.) Blood-sugar Levels.—The results of the mean 6 a.m. level of blood sugar for the group of successes and failures, averaged over five days without insulin, together with the mean reduction in blood-sugar level averaged over the five days following the administration of BZ 55, are summarized in Table VI, and

TABLE VI.—*Effect of BZ 55 on Fasting (6 a.m.) Blood-sugar Levels*

	6 a.m. Blood-sugar Level Before BZ 55 (mg./100 ml.)		Reduction in Blood-sugar Level After BZ 55 (mg./100 ml.)		No. of Cases
	Mean	Range	Mean	Range	
Successes	215	132 to 275	73	15 to 132	16
Failures	267	123 ,, 421	29	−60* to 150	18

*−, Increase in blood-sugar level.

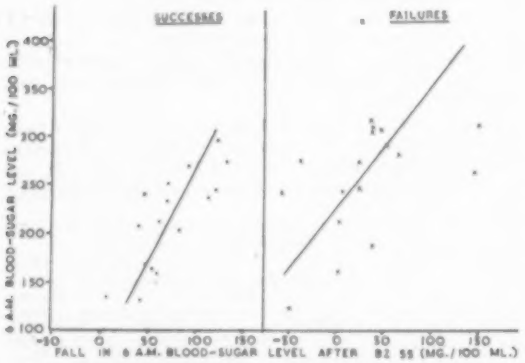

FIG. 1.—Effect of BZ 55 on fasting blood-sugar level.

expressed graphically in Fig. 1. The correlation between the 6 a.m. mean blood-sugar level before treatment and its reduction after treatment is statistically significant ($P<0.01$), and the mean 6 a.m. blood-sugar level is higher among the group of failures than among the group of successes ($P<0.05$). When the regression on initial blood-sugar level is allowed for, the fall in the 6 a.m. blood-sugar level after BZ 55 is significantly greater ($P<0.01$) in successes than in failures.

There is therefore, in general, a fall in the resting blood-sugar level of the failures after BZ 55 administration, but it is less pronounced than that observed in the successes, and, in view of the higher mean initial levels in the former, their blood sugar levels are not reduced to within the normoglycaemic range.

Effect of BZ 55 on the Postprandial (2 p.m.) Blood-sugar Levels.—The results of the mean 2 p.m. level of blood sugar for the two groups of patients averaged over five days without insulin, together with the mean reduction in blood-sugar level averaged over the five days following BZ 55 administration, are summarized in Table VII. An analysis of variance revealed no correlation between the fall in blood sugar after BZ 55 and the mean level before administration, which is in contradistinction to the results for fasting (6 a.m.) levels. The average blood-sugar level at

TABLE VII.—*Change in Postprandial Blood-sugar Levels (2 p.m.) After Administration of BZ 55*

		2 p.m. Blood-sugar Level Before BZ 55 (mg./100 ml.)	Reduction in Blood-sugar Level After BZ 55 (at 2 p.m.) (mg./100 ml.)	No. of Cases
Successes	Mean	272	87	15
	Range	165 to 376	171 to 37	
Failures	Mean	354	−182*	18
	Range	176 to 474	197 to −182	

*−, Increase in blood-sugar level.

2 p.m. before treatment is lower for the successful group than for the failures ($P=0.01$), and the reduction in blood sugar is greater in the former group than in the latter ($P=0.01$).

Mean Rise in Blood-sugar Levels from 6 a.m. to 2 p.m. Before and After Administration of BZ 55.—This analysis was undertaken to determine the effect of BZ 55 in controlling the postprandial rise in blood-sugar levels. The average of the mean initial blood-sugar levels at 6 a.m. before and after treatment, and the corresponding average of the mean difference between the 2 p.m. and 6 a.m. blood-sugar levels are shown in Table VIII. There is no regression

TABLE VIII.—*Mean Rise in Blood-sugar Levels from 6 a.m. to 2 p.m. Before and After the Administration of BZ 55*

		6 a.m. Blood-sugar Level (mg./100 ml.)		Increase in Blood-sugar Level at 2 p.m. (mg./100 ml.)		No. of Cases
		Before BZ 55	After BZ 55	Before BZ 55	After BZ 55	
Successes	Mean	211	140	55	46	15
	Range	132 to 298	89 to 197	0 to 164	3 to 107	
Failures	Mean	267	238	83	118	18
	Range	123 to 421	119 to 396	−3* to 167	−140* to 408	

*−, Decrease in blood-sugar level.

of the postprandial rise in blood-sugar level on the 6 a.m. level; the mean 6 a.m. level is lower after BZ 55 administration (successes, $P=0.001$; failures, $P=0.05$); the mean blood-sugar level of the failures is higher at 6 a.m. than that of the successes ($P=0.001$). The most important finding, however, is the lack of a significant difference between the postprandial rise before and after treatment with BZ 55 and the fact that this rise is greater in the group of failures than in the group of successes ($P=0.01$). Furthermore, the postprandial rise is more variable in the group of failures after treatment with BZ 55 than before ($P<0.002$). These findings suggest that BZ 55 exerts no action on the utilization of exogenous glucose and that it therefore may control the mechanisms of gluconeogenesis, glycolysis, or glycogenolysis.

Acute Effect of BZ 55 on Blood-sugar Levels of Overnight Fasted Patients whose Fasting is Continued from 6 a.m. to Midday.—The methods previously outlined for the two-day test were used and the mean 6 a.m. level of blood sugar following the administration of BZ 55 is recorded in Table IX. There is a positive regression of the reduction of blood sugar after BZ 55 on the initial 6 a.m. level, which is shown in Fig. 2. When the reduction in blood-sugar level is corrected for the initial 6 a.m. level it is greater in the successful group than in the failures ($P=0.001$).

In addition the reduction in blood-sugar levels in the two-day test—that is, from 6 a.m. to midday—is greater than the mean reduction in fasting blood-sugar levels in the five days after administration of BZ 55 for the same patients.

TABLE IX.—*Acute Effect of BZ 55 on Blood-sugar Levels of Fasted Patients from 6 a.m. to Midday*

	6 a.m. Fasting Blood-sugar Level on Day BZ 55 was given (mg./100 ml.)		Amount by which Blood-sugar Level was Reduced 6 Hours after Administration of BZ 55 (Midday) (mg./100 ml.)		No. of Cases
	Mean	Range	Mean	Range	
Successes ..	224	129 to 303	116	49 to 197	15
Failures ..	290	119 to 450	123	−15 to 249	14

Effect of BZ 55 on Glycosuria.—The mean of the amounts of glucose in 24-hour samples of urine (6 a.m. to 6 a.m.) for the five days prior to the administration of BZ 55, and the amount by which the glucose excretion is reduced in a corresponding period after treatment with BZ 55, are summarized in Table X. There is a positive regression of the reduction of glycosuria on the mean level before treatment

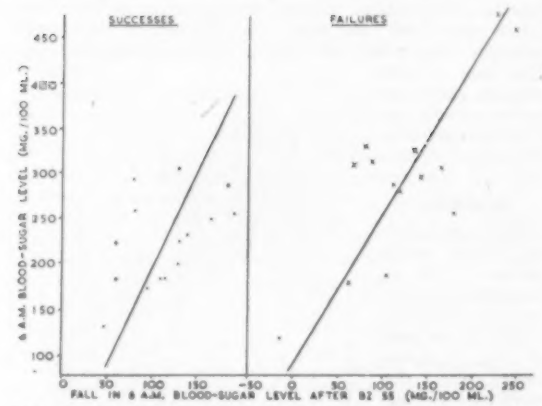

FIG. 2.—Effect of BZ 55 on 6 a.m. blood-sugar level. (Two-day test.)

with BZ 55 ($P=0.001$), and when the reduction of glycosuria is corrected for the mean initial level it is more pronounced in successful cases than in unsuccessful cases ($P=0.01$). The regression is shown in Fig. 3, and the high degree of correlation for the successful group is clearly evident. In nearly every instance there is virtually no glycosuria in the successful group following treatment with BZ 55.

TABLE X.—*Effect of BZ 55 on Glycosuria*

	Amount of Glucose Excreted in 24-hour Samples of Urine before BZ 55 Administration (g.)		Reduction in Amount of Glucose Excreted in 24-hour Samples of Urine after BZ 55 Administration (g.)		No. of Cases
	Mean	Range	Mean	Range	
Successes ..	30·4	1·3 to 82·6	23·8	1·3 to 77·0	15
Failures ..	61·3	26·8 to 116·3	19·8	−16·5* to 57·1	15

*−, Increase in amount excreted.

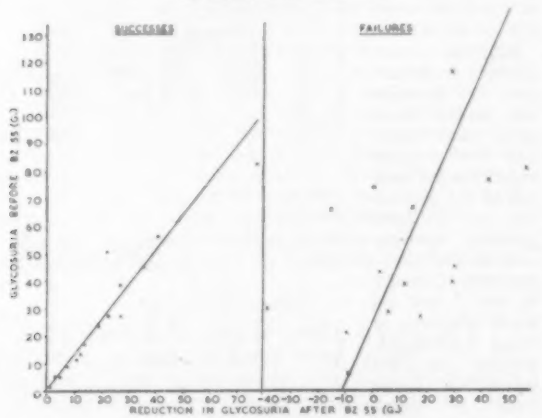

FIG. 3.—Effect of BZ 55 on glycosuria.

Change in Volume of Urine Excreted and in Glycosuria Following Administration of BZ 55.—There is a reduction in the mean volume of urine excreted in both the successes and the failures which is not statistically significant (see Table XI). This is not surprising in view of the wide range in the volumes of urine excreted. There is no correlation between the change in urine volume and reduction in glycosuria in the successful group, but there is a significant correlation in the group of failures ($P=0.001$). These differences in correlation are evident in Fig. 4. In the group of failures, therefore, the smaller the volume of urine excreted in 24 hours after BZ 55 the less sugar will that sample contain. The lack of correlation in the group of successful cases may be due to too small a number tested and a narrower range in quantity of urine excreted.

TABLE XI.—*Change in Volume of Urine Excreted and in Glycosuria Following Administration of BZ 55*

	Change in Volume of Urine Excreted after BZ 55 (ml.)		Reduction in Glucose Content of Urine after BZ 55 (g.)		No. of Cases
	Mean	Range	Mean	Range	
Successes ..	−199	−943 to 350	21·4	1·3 to 77·0	15
Failures ..	−248*	−1,080 to +463	12·8	−38·6† to 57·1	13

*−, Decrease in volume. †−, Increase in amount (g.).

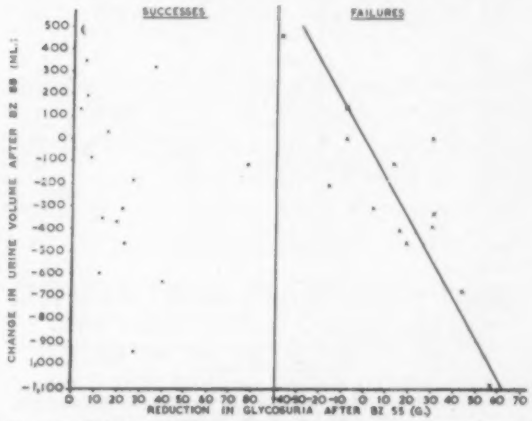

FIG. 4.—Relationship between the change in volume of urine excreted and glycosuria after BZ 55.

Blood and Urine Sulphonamide Levels.—On the first group of 12 patients the blood sulphonamide levels on the day of the two-day test were estimated at hourly intervals after the dose of BZ 55; they showed a steady rise up to six hours in each patient. The blood sulphonamide levels at one hour and six hours after the treatment with BZ 55 are shown in Table XII. It can be seen that there are no differences between the levels of the successful cases and those of the failures. On all the other patients the blood sulphonamide levels were estimated on the day of the two-day test at six hours after the dose of BZ 55. The average level for free sulphonamide at this time was 11.9 mg. per 100 ml. for successes and 11.4 mg. per 100 ml. for failures, whilst the corresponding levels for conjugated sulphonamide were 0.8 mg. and 0.9 mg. per 100 ml. respectively. There was

TABLE XII.—*Blood Sulphonamide Levels on the Day of the Two-day Test*

Time		6 Successful Cases		6 Failures	
		Blood Sulphonamide (mg./100 ml.)		Blood Sulphonamide (mg./100 ml.)	
		Free	Conjugated	Free	Conjugated
1 hr. after BZ 55	Range	5–10	Nil	5·2–8·7	Nil
	Mean	6·9		7·0	
6 hrs. after BZ 55	Range	9·5–11·7	0·8–2·5	9·5–11·7	0·8–2·3
	Mean	10·65	1·48	10·6	1·56

TABLE XIII.—*Excretion of Total Free and Conjugated Sulphonamide in 24-Hour Specimens of Urine in Patients Receiving a Maintenance Dose of 1 g. BZ 55 Daily*

	Mg. of Sulphonamide Excreted 24 Hours		Ratio Free: Conjugated	No. of Cases
	Free	Conjugated		
Successes	468	180	2·60	13
Failures	325	348	0·93	10

no significant difference between the levels in either group. On maintenance doses of BZ 55 the blood sulphonamide levels six hours after 1 g. of BZ 55 ranged from 7.7 to 12.5 mg. per 100 ml. (mean 11.7 mg.), and eight hours after, from 8.7 to 23 mg. per 100 ml. (mean 13.6 mg.).

The total amount of free and conjugated sulphonamide excreted in 24-hour specimens of urine was also estimated

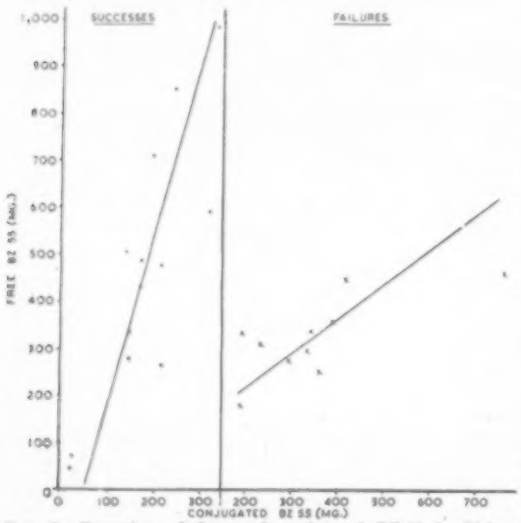

FIG. 5.—Excretion of free and conjugated BZ 55 in 24-hour specimens of urine when patients are receiving a maintenance dose of 1 g. of BZ 55 daily.

for patients during the in-patient period when they were receiving a maintenance dose of 1 g. of BZ 55 each day. On analysis, the results, presented in Table XIII, show that there is a significant positive correlation between the amount of free and conjugated sulphonamide excreted ($P=0.01$); the excretion of conjugated sulphonamide is higher in failures than in successes ($P<0.01$) and the difference between the excretion of free sulphonamide in either group is not significant. The evidence for the regression is shown in Fig. 5.

Complications of Treatment

Skin reactions occurred in 5 out of 45 cases. In four cases BZ 55 was then replaced by N-(4-methyl-benzosulphonyl)-N'-butyl-urea (D 860), and the rash, a typical maculopapular sulphonamide rash, in each case gradually disappeared. No other complications have occurred in our series so far.

Examples of Successful and Failed Cases

Case A.—A woman, aged 72. Diabetes was first diagnosed in November, 1955, following gradual onset of thirst, polyuria, lassitude, and loss of weight. On 20 units of insulin zinc suspension her urine was sugar-free. During the trial period in the ward without insulin her urine showed heavy glycosuria; her fasting blood sugars were over 200 mg. per 100 ml. and her postprandial blood sugars over 300 mg. per 100 ml. She was, however, symptom-free and had no acetonuria. The test dose of BZ 55 led to a marked drop in the blood sugar, and subsequently a maintenance dose of 1 g. daily cleared the urine of sugar and lowered her blood-sugar levels. This was an example of a successful replacement of insulin by BZ 55 as shown in Fig. 6.

Case B.—A woman aged 57. Diabetes was diagnosed six years previously, following a history of thirst and polyuria. Her diabetes had been controlled on 30 units of protamine zinc insulin daily. She was admitted to the ward and her insulin discontinued for five days. During this period she showed heavy glycosuria and acetonuria. BZ 55 was administered and caused some fall in the blood sugar the first day, but after that blood and urine sugars rose steadily on 1 g. a day. Trebling of dose to 3 g. daily did not reverse this trend; she began to complain of thirst and polyuria. Insulin was reinstituted, with rapid improvement. This was an example of failure to replace insulin by BZ 55 as shown in Fig. 7.

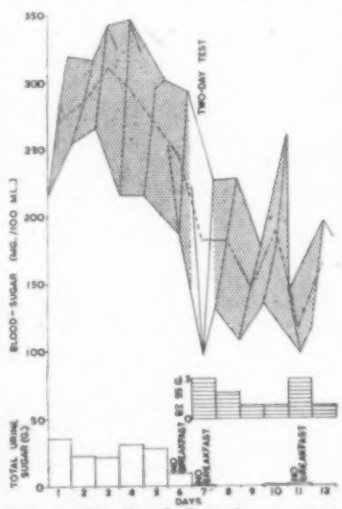

FIG. 6.—Details of Case A, a woman aged 72. (Success.)

Discussion

The fasting blood-sugar level would appear to be an important factor in assessing the effect of BZ 55. In none of our successful cases was this more than 275 mg. per 100 ml. While these patients were in the ward, on a measured diet but without insulin, they showed raised blood sugars and considerable glycosuria. There was, however, no acetonuria; thirst and polyuria were slight. They might thus be described as mild diabetics, and a maintenance dose of 1 g. daily was successful during the period of observation in keeping their blood level normoglycaemic and the urine free of sugar.

BZ 55 proved ineffective in the control of diabetics who easily developed acetonuria. The fasting blood sugars ranged from 123 to 421 mg. per 100 ml. In some patients substitution of the morning dose of insulin by BZ 55 had led by the afternoon to rising blood sugars, acetone in the urine, and symptoms of thirst, necessitating administration of insulin. These were young diabetics normally difficult to control. In the remainder of the failed cases the test dose of BZ 55 caused a significant drop from the fasting blood-sugar level, but subsequent maintenance therapy failed to prevent hyperglycaemia and glycosuria, and in some there was gradual onset of thirst, polyuria, and loss of weight. Trebling the dose of BZ 55 did not reverse this trend.

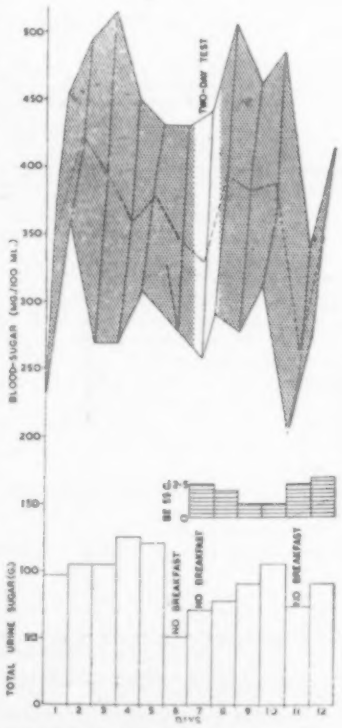

FIG. 7.—Details of Case B, a woman aged 57. (Failure.)

Failure to control these severe or moderately severe diabetics on oral therapy alone does not exclude the possibility

that BZ 55 given in conjunction with insulin might reduce the amount of insulin required or might lead to an easier control in unstable patients; these problems were not investigated.

The response of patients to BZ 55 was not related to the duration of their diabetes or to the incidence of complications. In the group of successes, however, there was generally a history of diminishing insulin requirements, while in the failures the need for insulin was greater, and had, if anything, increased with the progression of the disease. It may be that in the successful cases with mild diabetes BZ 55 acted either by stimulating the secretion of endogenous insulin or by preventing its destruction, while in the failed cases there was insufficient endogenous insulin.

In 39 cases the initial dose of BZ 55 produced hypoglycaemia which was greater than that produced by any subsequent dose. This suggests that following the initial dose the available insulin, or the mechanism regulating its use, was quickly exhausted in those diabetics who subsequently failed to respond.

BZ 55 exerted no control in either group over the postprandial rise in blood sugar. Its action is therefore probably on the mechanism controlling the utilization of endogenous glucose. With that in view, in all patients maintained on BZ 55 stress has been laid on the importance of adhering to the dietary regime.

German workers have indicated that BZ 55 and D 860 are most likely to be successful in obese diabetics. The present study showed the mean deviation in body weight in the group of successful cases to be slightly lower than the ideal weight, with only one case of gross obesity. This indicates that the drug can act as successfully in underweight patients as in those who are normal or overweight. During their period as in-patients, body weight did not alter significantly once BZ 55 therapy had begun.

Kinsell *et al.* (1956) found in two severe diabetics that the greater part of the sulphonamide excreted in the urine was conjugated in the patient treated successfully by BZ 55, whereas the greater part of the urinary sulphonamide was in the free state in the patient who failed to respond. The present investigations were at variance with this, since it was found that the excretion of conjugated sulphonamides was higher in the failed cases than in the successes.

Skin reactions occurred in 11% of the cases, but gradually disappeared when the patients were transferred to D 860. In view of these toxic manifestations, and the possibility of other adverse effects which may appear, particularly in the blood or liver, caution must be exercised before deciding to treat a patient with these drugs. Finally, it must be stated that the mode of action of BZ 55 remains unknown, as does its influence on the complications in the vessels, kidneys, and eyes which occur in long-term diabetes.

For these reasons BZ 55 must not be regarded as having reached therapeutic status in the management of the diabetic patient.

Summary

The response to the administration by mouth of BZ 55 tablets was studied in a group of 45 diabetics normally requiring insulin. These studies were undertaken under conditions of controlled diet on in-patients.

Diabetics in whom the drug was successful often had a history of diminishing insulin requirements. In no instance was the fasting blood-sugar level greater than 275 mg. per 100 ml., and the fasting range was from 123 to 275 mg. per 100 ml.

Diabetics in whom the drug failed tended to have a higher insulin requirement than the previous group. The fasting blood sugars ranged from 123 to 421 mg. per 100 ml. and there was a tendency to acetonuria.

BZ 55 does not exert any influence over the postprandial rise in blood sugars, either in the group of successes or in the failures.

There is no difference in levels between free and conjugated sulphonamides in the blood between successes and failures. In the urine there is more excretion of conjugated sulphonamides in the failed cases than in the successful ones.

Five patients (11%) developed skin reactions due to the drug.

Our thanks are due to Dr. K. Thomson for his help in the wards; to Mrs. Collins for the supervision of the diets; to Mr. Garfield for unstinting support with the biochemistry; to the ward staffs; and to Messrs. J. V. Smart, T. Hobson, R. Neville, P. Roberts, D. Sutton, and J. Trethewey, of the Biological Control Laboratories, the Wellcome Foundation, for invaluable assistance with the biochemical and statistical analyses. We also thank the British Insulin Manufacturers for supplies of BZ 55 and Professor Ehrhardt, of Hoechst A.G., for D 860.

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CLINICAL TRIAL OF THE NEW ORAL HYPOGLYCAEMIC AGENT BZ 55

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The discovery of the hypoglycaemic action of certain sulphonamide preparations, and their use in the treatment of diabetes, has recently been the subject of a number of publications on the Continent, notably in Germany (Bertram *et al.*, 1955; Franke and Fuchs, 1955; Loubatières, 1955; Quilley, 1955). The drug most commonly used has been N-butyl-N′-sulphanilylurea (BZ 55, "nadisan," "carbutamide"), and the preliminary results obtained in a clinical trial of this substance in the Diabetic Department at King's College Hospital are briefly described.

In the absence of reliable information on the clinical type of diabetes and on the influence of diet in the cases treated in Germany and elsewhere, it was decided first to give BZ 55 to a small series of representative diabetics, with the object of correlating such broad clinical distinctions as age, severity, insulin requirement, and duration of the diabetes with responsiveness to the drug. From the results so obtained it was hoped that a group or groups of patients could be selected for treatment in the out-patient department; this policy was largely dictated by lack of beds.

Clinical Material

Representative Group.—A group of 21 patients were selected to cover a wide range of age, weight, and severity and duration of diabetes for the purpose outlined above; eight of these were in-patients.

Selected Group.—A group of 17 patients were treated in the out-patient department, the criteria for selection being based on results obtained in the representative group.

Methods

Diet control consisted of measured carbohydrate, with free protein and fat, and was accurate in hospital. Out-patients had previously received detailed instruction in diet, and, because none were gaining weight, they were presumed to be adhering to it within reasonable limits. Since a new treatment often leads to more rigid adherence to diet than usual, the patients were first studied for a control period of two weeks while receiving dummy tablets. In some subjects receiving insulin the dose was not changed during the trial; in the others insulin was discontinued at least one week before BZ 55 was given. All patients were weighed twice weekly. On the first and second days of the trial patients were given respectively 2.5 and 1.5 g. of BZ 55, the dose on subsequent days being 1 g. In patients who failed to show a satisfactory response by the seventh day the maintenance dose was gradually increased.

The total excretion of glucose in 24 hours was estimated daily in in-patients and twice weekly in out-patients. Capillary blood-sugar estimations were made by a modified Nelson technique at least three hours after breakfast, and at the same time on each occasion. In the group of 17 out-patients night and early morning specimens of urine were tested for sugar and acetone bodies, and the blood sugar was estimated at varying times after breakfast, but not less than two hours.

Results

Representative Group.—The results obtained in the group of representative diabetics are summarized in Table I. The response to BZ 55 was recorded as good, moderate, or no response, according to whether the glycosuria disappeared completely, was reduced in amount, or was unaffected. In nine cases the response was good, in six moderate, and in six there was no response. In the nine cases classified as good the age of onset varied from 46 to 70 years, in the six moderate from 45 to 75, and in five of the six with no response from 9 to 46, the remaining failure being 65. Seven of the nine successes never required insulin, one was on 12 units and one on 48 units. In the moderate group four needed no insulin, the remaining two having been on 24 and 34 units respectively. Of the six who showed no response three had never had insulin, one being a child of 12 with diabetes of recent onset and severe ketosis; the remaining three needed relatively large doses of insulin. The cases with heavy ketonuria failed to respond to BZ 55. Of the 15 patients who showed a good or moderate response to BZ 55, the minimum age of onset of diabetes was 45, and maximum duration 22 years. Only four cases required insulin, the maximum period of insulin therapy being 18 years. No case showed ketonuria even after withdrawal of insulin.

Selected Group.—The results obtained in the group of 17 selected out-patients are summarized in Table II. All patients in this group developed diabetes after the age of 40, the range being 41 to 76; none showed significant ketonuria without insulin, and none were grossly overweight. In all cases diet alone failed to control glycosuria. In this group there was a good or moderate response to BZ 55 in every case, the final blood sugar being less than 180 mg. per 100 ml. in 11, between 180 and 200 mg. in three, and between 201 and 250 mg. in the remaining three cases. Insulin was replaced in three patients and avoided in two suffering from poor vision. Eight patients had previously been on insulin, the dosage varying between 12 and 88 units; the response was good in four and moderate in four, including the only two previously on large doses of insulin.

Toxic Reactions.—Transient giddiness occurred in five patients within two hours of the initial dose of BZ 55 and

TABLE I.—*Effect of BZ 55 in 21 Representative Diabetics*

Case No.	Sex	Diabetes: Age at Onset	Diabetes: Duration (Years)	Diet G. Carb.	Insulin	Ketosis	BZ 55: Max. Daily Dose	BZ 55: Total Days	Weight in lb.: At Start	Weight in lb.: Alteration	Blood Sugars (mg./100 ml.): Initial	Blood Sugars (mg./100 ml.): Final	Urine Glucose (g./Day): Initial	Urine Glucose (g./Day): Final	Remarks
							No Response								
1*	M	14	25	250	92 u. S.I. cont.	0	2 g.	27	123	+3	173	212	39·4	69·7	Skin rash
2*	M	36	7½	250	72 ,,	0	3 ,,	29	173	+2	93	141	37·3	63·2	
3*	F	9	5/12	180	0	0	2 ,,	9	63	0	275	477	47·4	68·1	
4*	F	12	0	180	0	+++ ($FeCl_3$)	1 ,,	7	84	0	380	331	183	157	
5	F	46	2/52	150	0	,,	3 ,,	20	150	−6	279	262	Not done		Glycosuria and ketosis throughout
6*	M	65	3½	180	44 u. I.Z.S. discont.	0	4 ,,	23	163	+1	231	276	42	57·5	
							Moderate Response								
7	F	57	3	90	0	0	1 g.	21	232	+5	341	131	196	6·3	
8	M	46	3/12	120	0	0	2 ,,	31	168	+4	302	152	122	12	
9	M	45	1½	120	0	0	3 ,,	62	160	+1	298	172	91·8	12·2	
10	F	75	2/52	100	0	0	1 ,,	28	138	+1	391	186	81·6	5·4	
11*	F	48	22	140	Since 1938 I.Z.S. 24 u. discont.	0	2 ,,	56	118	+2	294	146	55·1	6·6	
12	M	60	3½	160	I.Z.S. 34 u. discont.	0	2 ,,	14	162	+2	379	218	105	65	Persistent giddiness on 2 g. daily
							Good Response								
							Max. Dose	Days to Clear Glycosuria							
13	M	46	2/52	130	0	0	2 g.	1	178	+2	288	144	20	0	Initial ketosis cleared with diet
14	F	70	7	120	0	0	1 ,,	28	130	+2	298	165	43	0	
15	M	62	5	120	0	0	1 ,,	3	153	0	228	75	18·4	0	
16	M	68	2½	120	0	0	1 ,,	28	155	0	183	135	8·1	0	
17*	M	70	1/12	160	0	0	2 ,,	25	131	+3	292	106	69	0	Persistent giddiness
18	F	70	1/12	90	0	0	1 ,,	4	135	+1	217	110	55	0	
19	F	51	10½	100	0	0	2 ,,	22	153	0	284	154	74·3	0	
20	F	70	1½	160	I.Z.S. 12 u. discont.	0	1 ,,	3	119	0	230	166	35·9	0	
21*	F	67	3½	90	48 u. discont.	0	2 ,,	28	150	Oedematous	320	145	30·8	0	Recovering from heart failure

* Patient in hospital.

lasted for about 15 minutes, but did not recur. Severe giddiness which persisted until the drug was stopped or the dose reduced occurred in three cases. In two cases there was an irritant erythematous rash which rapidly disappeared on stopping treatment. One out-patient developed a severe papular sulphonamide rash with some purpuric haemorrhages, and typical sulphonamide drug fever occurred in one case.

Sensitivity Test.—In view of the uncertainty of the clinical response to BZ 55 in diabetes it was decided to investigate the hypoglycaemic action of a single dose of the drug in a small series of patients. It was hoped that this type of sensitivity test might provide a useful guide in the selection of patients for treatment with BZ 55. The test was carried out on 16 patients and consisted in estimating the blood sugar in the fasting state and again four hours after a single dose of 50 mg. of BZ 55 per kilogram of body weight. A control test without BZ 55 was carried out on 11 of the 16 patients. The results of this investigation are shown in Table III. In patients known to respond to BZ 55 there was a significantly greater fall with than without the drug ($P = 0.001$). A fall of less than 30% was observed in 9 out of 11 control tests. After BZ 55 the fall exceeded 40% in eight patients; in two of the remaining three a dose of 2 g. of BZ 55 had been required to produce a satisfactory response.

Arteriovenous Difference.—This test of sensitivity to BZ 55 offered a convenient opportunity to investigate the effect of the drug on the peripheral utilization of glucose. Simultaneous capillary and venous blood-sugar estimations were carried out during the period of maximum hypoglycaemic response to BZ 55, but no significant increase in arteriovenous difference was demonstrated; this would seem to indicate that BZ 55 does not increase the peripheral utilization of glucose.

TABLE III.—*Results of a BZ 55 Sensitivity Test in 16 Subjects*

Case	Fall in 4 Hours' Fasting		Fall in 4 Hours after BZ 55		Known Reaction to BZ 55
	Initial B.S. Level (mg./100 ml.)	Fall %	Initial B.S. Level (mg./100 ml.)	Fall %	
1	250	26·4	254	52·0	Good
2	260	20·0	272	44·8	,,
3	242	21·9	187	56·2	,,
4	284	11·3	360	42·0	,,
5	275	16·8	329	35·0	Larger dose needed
6	279	11·2	342	29·8	,, ,,
7	237	8·9	226	19·5	Good
8	173	32·4	205	60·5	,,
9	236	25·4	250	57·2	,,
10	318	37·1	264	46·6	,,
11	143	25·2	157	45·2	,,
12			446	72·4	,,
13			205	47·8	,,
14			218	49·1	,,
15			274	18·2	Nil
16			320	20·3	,,

Discussion

From the results obtained in the first series of 21 diabetics, to some extent representative in respect of age, duration, and severity of diabetes and insulin requirement, certain broad conclusions may be drawn regarding the type of patient in whom the drug may be expected to have some hypoglycaemic action. The presence of significant ketonuria either in patients treated by diet alone or after the withdrawal of insulin was consistently associated with complete failure to respond to BZ 55. In general it appeared that young diabetics and those requiring more than small doses of insulin show little or no response, nor was there reliable evidence that the administration of BZ 55 to such patients decreased their insulin requirement; two young diabetics actually passed more sugar when the drug was

TABLE II.—*Effect of BZ 55 in 17 Selected Out-patients*

Case No.	Sex	Diabetes		Insulin	Ketosis	BZ 55		Weight in lb.		Glycosuria (Benedict)		Blood Sugar (mg./100 ml.)		Indication for BZ 55	Remarks
		Age of Onset	Duration (Years)			Daily Dose	Days	Control	Change	Initial	Final	Initial	Final		
1	M	44	14	P.Z.I. 16 u. since 1944 discont.	Sl. tr. (Rothera)	1 g.	7	229	+1	N++ / M+	Tr. / Tr.	225	152	Urinary infection	Infection cleared
2	F	44	7	P.Z.I. 14 u. previously	0	1 ,,	14	158	−1	N++++ / M++++	Tr. / 0	269	110		
3	M	41	4	N.P.H. 30 u. discont.	0	0·5 ,,	7	176	0	N tr. / M 0	0 / 0	157	104		
4	F	41	6	P.Z.I. 28 u. discont.	0	1 ,,	14	155	−2	N++++ / M tr.	++ / 0	205	125		
5	F	76	6	0	0	1 ,,	14	115	0	N++++ / M++++	Tr. / Tr.	334	200	Pruritus	Pruritus cleared
6	F	61	7	I.Z.S. 32 u. previously	0	1 ,,	14	170	+4	N++++ / M++++	++ / 0	301	176	Refused insulin	
7	F	67	6	0	0	1 ,,	14	126	+2	N++++ / M++++	+ / Tr.	350	214	,,	
8	F	60	3	I.Z.S. 72 u. previously	0	1 ,,	14	177	+2	N++++ / M+++	0 / Tr.	306	245		
9	F	52	7	0	0	1 ,,	14	147	+3	N++++ / M++	0 / 0	328	197	Pruritus	Pruritus cleared
10	F	63	1	0	Tr. Rothera	1 ,,	14	137	+3	N++++ / M+++	+ / 0	309	131	Nocturia	
11	F	55	13	0	,,	1 ,,	23	134	+4	N++++ / M+++	++++ / Tr.	290	200	Refused to diet	
12	F	49	7	I.Z.S. 12 u. cont.	0	0·5 ,,	14	123	+3	N 0 / M 0	0 / 0	326	179	Dislikes insulin	Giddiness on 1 g. daily
13	F	60	7	S.I. 88 u. previously	Tr. persisted	1 ,,	35	162	+3	N++++ / M++++	+++ / Sl. tr.	315	227	Pruritus	Pruritus improved
14	F	46	1/52	0	++ Rothera cleared	1 ,,	14	196	0	N+++ / M+++	0 / 0	175	94	Slight ketosis	Generalized irritant rash
15	F	66	5½	0	0	2 ,,	7	123	−1	N+++ / M++++	Tr. / V. sl. tr.	283	112	Loss of weight	
15a	Second course				++ Rothera cleared	1 ,,	14	121	+3	N++++ / M++++	Tr. / S. tr.	252	172		Weight increased
16	M	41	18	0	0	1 ,,	35	177	+3	N++++ / M+++	++ / +	245	157		
17	M	56	6	0	0	1 ,,	14	175	+3	N++++ / M++++	0 / 0	226	103		

given in addition to their normal daily dose of insulin. It follows that, when insulin is a vital necessity in treatment, any attempt to replace it by BZ 55 is almost certain to result in a serious relapse. It is of interest that no response was obtained in a child of 9 with diabetes of five months' duration who had never had insulin and whose urine contained no ketone bodies.

On the negative side no constant relationship could be demonstrated between the response to BZ 55 and the age of the patient, the duration of the diabetes, or the duration of insulin therapy. It seemed to be immaterial that in some of those who responded there had in the past been episodes of severe ketosis, associated with infection or other general conditions, the treatment of which required large doses of insulin.

The factors in the representative series of 21 patients most consistently related to responsiveness to BZ 55 were the age of onset of diabetes, over 40 years in all cases, and absence of more than minimal ketonuria while on dietary control without insulin. The second series of 17 patients was therefore selected on these criteria. All the patients in this group were treated in the out-patient department and all showed some response to BZ 55. This would seem to indicate that the criteria used for selection were, in a limited sense, reasonably correct, and lend support to the findings of others who have carried out more extensive therapeutic trials with BZ 55 (Symposium 1956a, 1956b).

Our thanks are due to Professor G. Gray, the late Dr. H. Whittaker, Dr J. A. Robertson, and other members of the staff of the Diabetic Department who co-operated in this trial, and also to Eli Lilly and Co. and Boots Pure Drug Co. for supplies of BZ 55.

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BZ 55 IN DIABETES

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This paper gives an account of the administration of BZ 55 (N-butyl-N′-sulphanilylurea) under controlled conditions to 20 diabetic patients. They were a carefully selected group of diabetics, 16 of whom came into the category of those who could not be satisfactorily controlled by diet alone but did not require large quantities of insulin and had never shown ketosis. Four required insulin to avoid ketosis. More extensive clinical studies on the effect of BZ 55 in severe diabetics and other investigations designed to shed light on the mode of action of this and other hypoglycaemic agents are at present in progress. These will be published later.

Methods

The patients given BZ 55 were in various groups. In Group 1 there were 10 in-patients who had blood-sugar estimations carried out thrice daily (fasting, at 4 p.m.—that is, four hours after lunch but before tea—and at 8 p.m., two hours after the evening meal) (Table I). The 24-hour urinary output of sugar was measured, and thrice daily a semi-quantitative test of urine for sugar ("clinitest") and for ketones ("acetest") was carried out. The patients' weights were measured at the same time each morning, with the patient fasting and having emptied bowel and bladder.

TABLE I.—*Summary of Clinical Data*

Case No.	I.P./O.P.	Sex and Age	Age of Onset of D.M. (Yr.)	% of Av. Wt.	Insulin (Units)	Diet (Cals.)	Family History	Response to BZ 55
1	I.P.	M 68	36	82	16–32	2,000	−	+
2	I.P.	F 62	61	80	20	2,000	−	+
3	I.P.	M 73	70	(Amputation)	20	1,900	−	+
4	I.P.	M 82	82	89	24	1,800	−	+
5	I.P.	F 56	52	89	Nil	1,500	−	+
6	I.P.	F 45	45	103	20	2,000	−	+
7	I.P.	F 51	51	120	Nil	1,200	−	+
8	I.P.	F 55	50	113	..	2,000	−	+
9	I.P.	F 68	63	111	16	2,000	−	+
10	I.P.	F 55	ca 48	110	52	1,000	−	+
11	O.P.	M 62	51	68	20	2,000	+	+
12	O.P.	M 71	66	105	Nil	2,000	−	+
13	O.P.	F 54	53	104	..	1,600	−	−
14	I.P.	M 54	ca 36	96	80	1,850	−	−
15	I.P.	F 40	34	96	44	2,000	−	−
16	I.P.	M 25	25	86	64	2,500	+	−
17	I.P.	F 58	56	75	Nil	1,500	−	+
18	O.P.	F 47	44	125	..	1,000	−	−
19	O.P.	F 55	41	87	128	2,000	−	+
20	O.P.	F 63	56	91	16	1,800	−	+

Diet was constant throughout the period of each trial and no insulin was given. When it was judged that no further improvement was being obtained by the dietary restrictions alone, or hyperglycaemia was increasing, BZ 55 was given. This initial period varied from two to ten days. A high "loading" dose of BZ 55 was given over the first three days, and then a dose of 0.5 g. twelve-hourly was maintained. Daily measurement of BZ 55 blood level was carried out on a specimen obtained before the morning dose of the drug was given. The length of time over which the response to BZ 55 was observed varied with several factors, in particular the patient's willingness to remain in hospital. In three cases the effect of withdrawal and subsequent readministration of BZ 55 was studied.

The response of three out-patients (Group 2) was similarly observed (Nos. 11–13, Table I), the criteria in these cases being 24-hour urinary sugar outputs three or four times a week, with blood sugars measured three or four times a week on specimens taken at the same time each day. These patients tested their urine for sugar by clinitest regularly at home and their weight was measured on each visit to hospital. A control period of two weeks was established when, unknown to the patients, dummy tablets identical in appearance with BZ 55 tablets were administered. A minimum period of two weeks was studied to learn the effect of the drug.

An attempt was made to determine the efficacy of BZ 55 in a third group of three patients (Nos. 14–16, Table I) in whom previous study had shown that they undoubtedly required insulin to remain free from ketosis. In these cases BZ 55 was given in addition to a constant dose of insulin. With this exception observations were carried out as in Group 1. A minimum of five days' steady control was obtained before adding BZ 55 to the regime of diet and insulin.

Finally, in Group 4, consisting of one in-patient and three out-patients (Nos. 17–20, Table I), BZ 55 was used simply as a "therapeutic" agent, the response being judged by three daily semi-quantitative urine tests for sugar by clinitest. Of the three out-patients one was ill-controlled on diet alone, having sporadically in the past been given up to 16 units of insulin a day; the second was an insulin-resistant diabetic on 128 units of insulin a day (and this dose remained constant); and the third, an obese (125% of average weight) 47-year-old diabetic with heavy glycosuria despite an advised

diet of 1,000 calories. The in-patient was an elderly mild diabetic requiring insulin during the stress of a leg amputation for diabetic gangrene.

With Cases 14, 15, 16, and 19 the insulin dosage quoted is that given at the same time as BZ 55. With the remainder the dose of insulin is that on which the patient was controlled prior to the trial.

In all these cases the blood sugar was measured by the Hagedorn–Jensen method, urinary sugar by the quantitative Benedict method, and blood BZ 55 by the method adapted by King (1951) from the procedure of Bratton and Marshall (1939).

In addition to the procedures outlined above, the effect of BZ 55 on the arteriovenous difference in blood sugar was investigated. Six patients were studied, one on two occasions. In these instances the sugar estimations were done in duplicate by the Somogyi–Nelson method. Capillary blood was used as equivalent to arterial blood in glucose content, and venous blood was drawn from the dependent arm without stasis being induced by a tourniquet.

Results

In each of the first 16 patients (Table I) the mean blood-sugar level (usually the fasting level, unless otherwise stated) before and during treatment with BZ 55 was calculated and the significance of the fall in blood sugar determined. Only Group 1, with 10 patients, however, was large enough for further analysis. The mean fasting blood sugars of this group are shown in Fig. 1. In all but the last patient, the fall in fasting blood sugar on BZ 55 treatment was highly significant, as was also the mean fall for the whole group, shown in the final pair of columns.

A superficial inspection of these data suggests that, within the limits of the blood-sugar levels involved, the fall in blood sugar is greater when the initial level is high. On plotting the values for the fall in each patient against the initial level (Fig. 2, upper graph) there was, in fact, found to be a highly significant correlation ($P < 0.01$) between fall in blood sugar and the initial blood-sugar level. On the other hand, there was not a significant correlation ($P=0.1$) between the mean fasting blood-sugar levels before and during BZ 55 treatment (Fig. 2, lower graph). These two facts together indicate that, in the mild diabetic at any rate, BZ 55, in the dose used, lowers the fasting blood sugar from its initial level down to a level approximating the normal.

The effect of BZ 55 on the blood sugars of the three out-patients studied in detail (Cases 11–13) was statistically analysed in each case. In Cases 11 and 12 there was a clear-cut positive response to the drug. Case 13 did not respond. The fluctuation in blood-sugar estimations obtained made it clear that study of the effect of BZ 55 on out-patients was unrewarding.

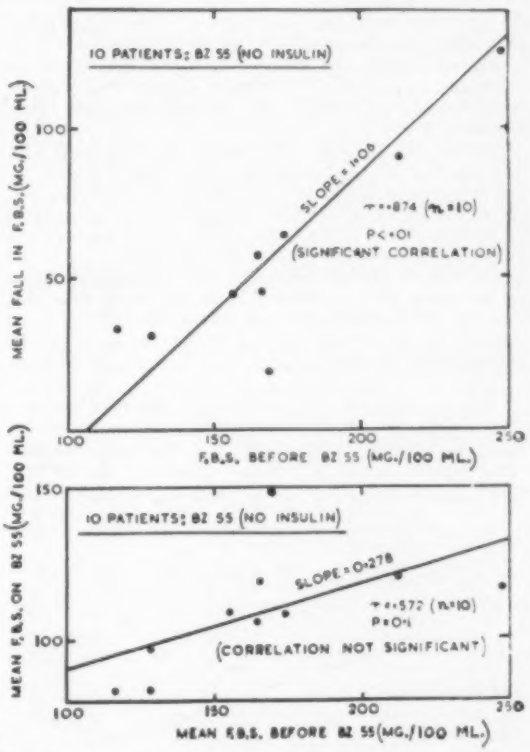

FIG. 2.—Correlation between (upper graph) mean fall in fasting blood-sugar on BZ 55 and initial fasting blood sugar, and (lower graph) mean fasting blood sugar on BZ 55 and initial fasting blood sugar.

Of the three patients (Cases 1, 7, and 10) in whom the effect of withdrawal of BZ 55 was studied, one (Case 1) relapsed in less than 72 hours, when there was still a BZ 55 blood level of 4.3 mg./100 ml. (Fig. 3). The other two took 9 and 15 days respectively before blood-sugar levels tended to rise.

The fasting blood sugars in Case 3 are recorded in Fig. 4 and compared with the BZ 55 blood level. With this patient a better response was noted when the large initial dose of BZ 55 was given than when the maintenance level was reached. Subsequently the maintenance dose was doubled to 1 g. twice daily, with the described effect.

One patient (Case 7) was readmitted six weeks after her initial trial of BZ 55. A mild diabetic, she had a good response and was discharged taking 0.5 g. twice daily. Gradually her diabetic symptoms, especially pruritus vulvae, returned. On readmission there was some improvement on the more exact in-patient 1,200-calorie diet. Satisfactory control, however, was obtained only on doubling the maintenance dose to 1 g twice daily.

A statistical analysis of the fasting blood sugars of Cases 14, 15, and 16 is shown in Table II, in which the figures obtained when the patients were on insulin alone are compared with those obtained when BZ 55 was given in addition to the same or smaller dose of insulin. It will be seen that two of the three patients had very high initial blood sugars, which were reduced only to the 180–200 mg./100 ml. level by BZ 55. In this group, too, it will be seen that, although

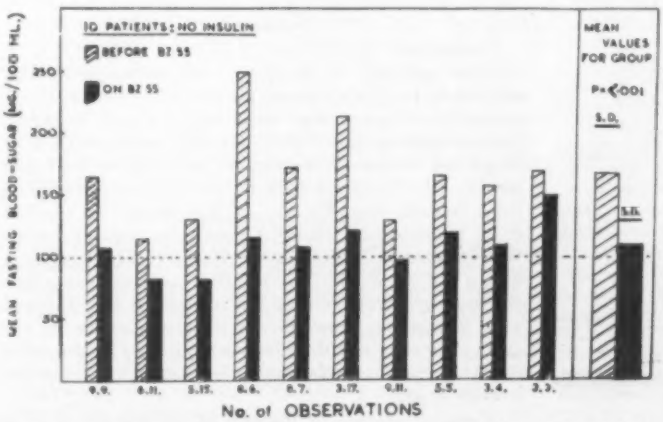

FIG. 1.—Effect of BZ 55 on diabetics maintained on diet alone (Cases 1–10).

the fall in blood sugar on BZ 55 is of the same order as in the first group, in no case is it significant. This is due to a greater fluctuation in blood-sugar levels in the insulin-treated group. Further analysis of this group is, of course, impossible until the numbers have been increased.

Case 15 is of interest. This patient was reasonably well controlled on 44 units insulin zinc suspension (I.Z.S.) daily. The reduction of this to 36 units resulted in ketosis developing within 24 hours. After she had been on 44 units of I.Z.S., with BZ 55 in addition, insulin dosage was reduced once more to 36 units. The patient was seven days on this regime without ketosis developing. The stoppage of BZ 55 on the eighth day was followed by ketosis on the ninth day, when the BZ 55 blood level was 4.6 mg. per 100 ml.

With the therapeutic use of BZ 55 in Cases 17–20, glycosuria was cleared in Cases 17 and 20 and, subjectively and by urine tests, control was better in Case 19. There was no apparent response to the administration of BZ 55 in Case 18.

No constant effect of BZ 55 on the arteriovenous difference of blood sugar was found. A decrease in the difference occurred as often as an increase.

No change in weight was noted in spite of improvement in control.

Toxic Effects.—Two widespread and fairly typical sulphonamide skin rashes occurred. One cleared with the administration of antihistamines, and the other with the cessation of the drug. Two patients were mildly nauseated on high dosage.

TABLE II.—*Effect of BZ 55 on Insulin-maintained Diabetics*

Case No.	Treatment		Mean F.B.S.	n	t	P	Significance
	BZ	Insulin					
14	Before	80 u. I.Z.S.	135	6	1·94	0·08	–
	On	80 u. I.Z.S.	90	6			
15	Before	44 u. I.Z.S.	320	5	1·70	0·1	–
	On	36 u. I.Z.S.	211	8			
16	Before	84 u. I.Z.S.	274	6	1·54	0·15	–
	On	64 u. I.Z.S.	181	7			

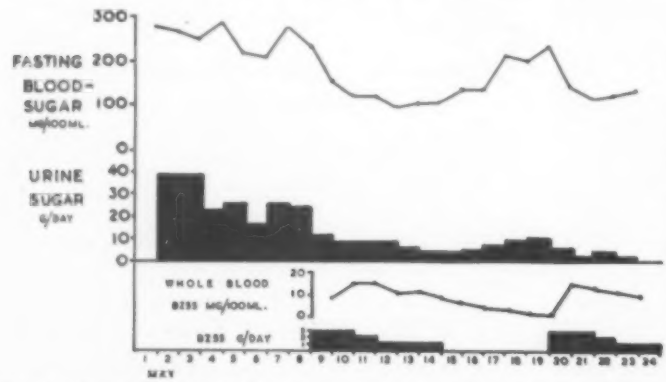

FIG. 3.—Case 1. Height 63 in. (160 cm.), weight 118 lb. (53.5 kg.). Effect on fasting blood sugar of stoppage and subsequent readministration of BZ 55, with concurrent BZ 55 blood levels.

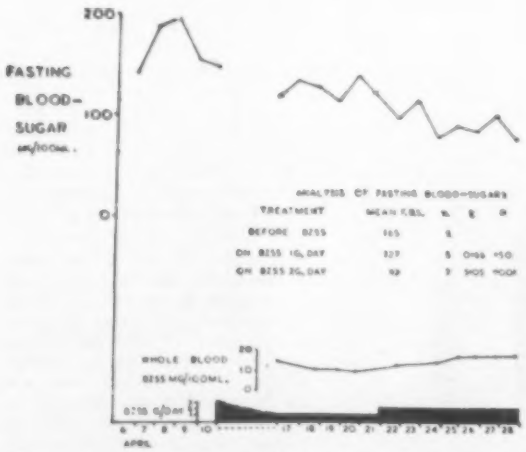

FIG. 4.—Case 3. Effect on fasting blood sugar of doubling the dose of BZ 55, with concurrent BZ 55 blood levels.

Discussion

Statistical analysis of the data derived from the 10 patients in group 1 would lead to the following conclusions. BZ 55 would appear to have a "normalizing" effect on the blood-sugar levels of these mild diabetics, and the higher the initial fasting blood-sugar levels found the greater the effect. The effect does not seem to be due to an increased sensitivity to insulin.

The study of the effect of BZ 55 on the arteriovenous difference of blood sugar, and other unpublished observations we have made on serum inorganic phophorus levels, would support this conclusion. In the more severe diabetics the fall in fasting blood sugar on BZ 55 was not statistically significant, and a larger group will have to be studied.

We can deduce no evidence in support of the contention that the drug is active only in overweight diabetics. The duration of the diabetic state has no correlation with the responsiveness of the patient. It is already evident from our limited experience of the drug that, although a satisfactory fall of blood-sugar and urine-sugar levels will occur in hospital on a carefully controlled diet, patients can relapse on a more liberal out-patient regime. In three of our patients it is now evident that 2 g. of BZ 55 is required daily to maintain a satisfactory clinical response. We have as yet no definite proof of the development of tolerance.

The fact that BZ 55 has already been shown to have toxic effects (Duncan, Baird, and Dunlop, 1956), and that it is also of course an antibacterial substance, is a challenge to the synthetic chemist to produce something better. Whether this compound proves ultimately to have a place in therapeutics or not, a laboratory tool of great importance is now available, and already new vistas in the intermediate metabolism of carbohydrate are appearing.

Summary

Results are reported of a clinical trial of BZ 55 on 20 diabetic patients, 14 of whom were in hospital. Ten mild diabetics, not satisfactorily controlled by diet alone, were studied under basal conditions and then on BZ 55 therapy and the same diet. Detailed measurements of blood and urine sugar were made, as well as of the blood level of BZ 55 and the daily weight. Three out-patients were studied similarly but in less detail. A further three patients who required insulin to prevent ketosis were studied in hospital when taking insulin and when taking BZ 55 in addition, the diet remaining constant. A fourth group of four patients were given BZ 55 simply as a therapeutic agent, in one case in addition to 128 units of insulin, and the effects were judged by the relief of symptoms and the results of qualitative tests for urinary sugar.

Statistical analysis of the data of the first group of 10 mild diabetics showed that the BZ 55 had a normalizing

effect on the fasting blood-sugar levels. The higher the initial fasting blood sugar the greater was the hypoglycaemic effect obtained. The four patients receiving BZ 55 in addition to insulin had better control than when receiving insulin only, but the series is too small to achieve significance. Studies of arteriovenous blood-sugar differences and of the changes in serum inorganic phosphorus levels provided no evidence that BZ 55 increased the effectiveness of the peripheral action of insulin.

We are grateful to Mrs. H. M. McGregor and Miss L. Constable for their biochemical estimations.

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HYPOGLYCAEMIC SULPHONAMIDES IN TREATMENT OF DIABETES

BY

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Recent reports from Germany (Bertram *et al.*, 1955) have suggested that certain relatively non-toxic sulphonamides with a hypoglycaemic action may be of value in the treatment of diabetes mellitus. Because of the interest which has been aroused by these reports, the following preliminary account is being published. It deals with experience in a diabetic clinic where 24 patients have been treated with N-butyl-N′-sulphanilylurea (BZ 55, "carbutamide") for periods up to seven months.

The German workers found that this compound was most effective in middle-aged "stable" diabetics: stable, in this context, meaning that if patients were not receiving insulin although they were hyperglycaemic they did not develop ketosis, and if they were using insulin it could be stopped without any immediate rise of blood sugar or the development of ketosis. Diabetics of this type are often obese, and, believing obesity to be undesirable in diabetics, it is the practice in this clinic to endeavour to control the condition with a low-calorie diet with less than the usual proportion of carbohydrate. In most cases if the diet is followed for a few weeks weight is lost, the blood sugar falls, and symptoms and glycosuria disappear. In a few, although the weight comes down, hyperglycaemia, glycosuria, and occasionally some symptoms persist. In the past it has been necessary to use insulin to achieve normoglycaemia in these patients; recently we have been assessing the possible use of oral BZ 55 as an alternative.

Selection of Patients

Patients were selected for trial with BZ 55 on the lines indicated above. Of the 24 patients, nine were men. Ages ranged from 38 to 82 years (mean, 63), and the diabetes had been recognized for from 1 to 42 years (mean, 10). Nine patients had developed their diabetes before they were 45 years of age. Ten had received insulin at some time, and in six of these it was being taken in doses of 10 to 84 units a day up to the time of the trial of BZ 55. All except two of the patients had glycosuria when BZ 55 was started, six had mild diabetic symptoms, most commonly polyuria, and five had diabetic retinitis. No patient had at any time had any significant degree of ketosis, although mild ketonuria had previously been observed in two. Thirteen patients were underweight when treatment was started; the majority of the others were only slightly overweight. Prior to treatment, three blood-sugar estimations were made on consecutive weeks ("random blood sugar"—that is, taken during the clinic between 10.30 a.m. and 12 noon after a normal breakfast—method of Kingsley and Reinhold (1949) modified). The means of these pre-treatment blood sugars are shown in Fig. 1. Patients who were on insulin had this stopped and were put on a low-calorie and restricted carbohydrate diet. BZ 55 was not started until the blood sugar exceeded 200 mg. per 100 ml.

Technique of Treatment

In most cases treatment was started with 2.5 g. the first day, 1.5 g. the next day, and 1 g. a day subsequently. In a number of cases BZ 55 was preceded by two weeks on inert tablets. During the control period and first few weeks of treatment the patients were on a low-calorie and restricted carbohydrate diet (1,250 calories, 100 g. of carbohydrate, in 12 patients; 1,500 calories, 125 g. of carbohydrate, 5 patients; 1,750 calories, 150 g. of carbohydrate, 7 patients). When it became clear that the tablets were controlling the blood sugar, diet was increased in the underweight patients. Initially the patients were seen at weekly intervals for clinical assessment, weighing, blood and urine sugar tests, and estimation of blood sulphonamide (method of Bratton and Marshall, 1939). The maintenance dose ranged from 0.5 to 2 g. a day (Fig. 1). Two patients have been treated for seven months, four for six months, and most of the remainder for three months or more.

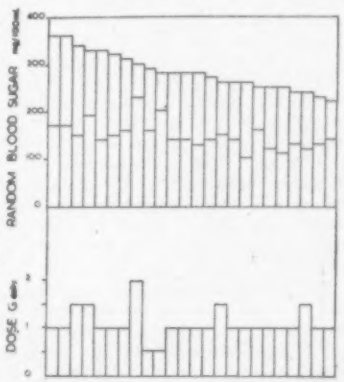

FIG. 1.—Mean pre-treatment and most recent "random blood-sugar" levels in each patient and maintenance dose of sulphonamide.

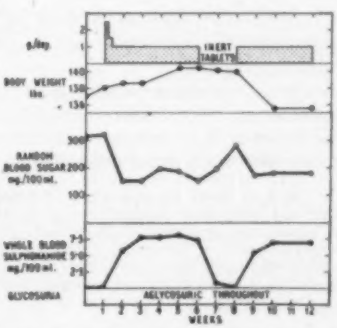

FIG. 2.—Man aged 56. Diabetes 12 years. No insulin. Diet 1,250 calories (92 g. carbohydrate). High renal threshold. Diabetic retinitis. Response to BZ 55 and effect of substituting dummy tablets for two weeks.

Results

Diabetic symptoms when present have been relieved and many of the patients claim to have felt better as their blood sugars have come down. No alteration has been observed in the retinitis. The reduction of blood sugar is shown in Fig. 1; with two exceptions the level is now satisfactory. In one of these the dose of BZ 55 (0.5 g. a day) is probably too low; the other patient has a blood sugar of 238 mg. per 100 ml. although she is taking 2 g. of sulphonamide daily. Lack of control in this case is thought to be due to unsatisfactory dieting. Only two patients continue to have glycosuria—one the uncontrolled patient just mentioned, and the other on account of a low renal threshold. BZ 55 was discontinued temporarily in six

patients and permanently in two, and within two weeks the blood sugar rose significantly (Fig. 2).

Eleven of the patients who were underweight before treatment have gained weight, six of the others have lost weight, and the remainder show no significant change. Whole-blood sulphonamide levels in patients taking 1 g. a day have been 5.2–9 mg. per 100 ml. (mean 6.7 mg. per 100 ml.)—expressed as sulphanilamide (to convert to whole-blood BZ 55 this should be multiplied by 1.7). Estimations on bigger doses suggest that the increase of blood level is less than expected and not directly proportional to the dose.

Side-effects.—Treatment had to be stopped after three and four weeks respectively in two cases on account of a widespread irritating rash. In one case there was a mild scaly eruption on the forehead which disappeared despite continued treatment. One patient developed mild hypothyroidism after five months' treatment with 1 g. a day; this has responded satisfactorily to treatment with L-thyroxine.

Discussion

Most middle-aged stable diabetics lose their symptoms if they keep to a low-calorie and restricted carbohydrate diet. In some, however, although the symptoms disappear, glycosuria and hyperglycaemia persist. Preliminary results suggest that in these cases the blood sugar can often be brought down with BZ 55. If the hyperglycaemia is the cause of such complications as retinitis and nephropathy, its control is of great importance to the patient. It will be of considerable benefit if this can be done by oral medication instead of insulin injections, which these patients, in the absence of symptoms, are not unnaturally reluctant to start. If, however, these complications are due to some other metabolic disturbance of the diabetes, there is no certainty that it will be influenced by the hypoglycaemic sulphonamides, and little is gained by prescribing them. Furthermore, it is still not known how these drugs work, and they may well prove to have dangerous toxic properties.

The hypoglycaemic sulphonamides are not "oral insulins" and have no place in the treatment of "insulin-deficient" diabetics. Diet remains the mainstay of treatment for the middle-aged diabetic with any tendency to obesity. The hypoglycaemic sulphonamides would seem to be indicated in only a comparatively small group. Until their value has been proved and their possible hazards more fully explored they cannot be recommended for widespread use.

Summary

A preliminary account is given of the use of a new hypoglycaemic sulphonamide in the treatment of diabetes mellitus.

Twenty-four stable middle-aged diabetics were chosen for treatment. Satisfactory reduction of the blood sugar was obtained in 23, but two had to be taken off the drug on account of a generalized rash.

We wish to thank the staff of the Routine Laboratories of the Courtauld Institute of Biochemistry of the Middlesex Hospital for the blood-sugar and blood sulphonamide estimations; Boots Pure Drug Company, of Nottingham, and Eli Lilly and Company, of Basingstoke, for supplies of BZ 55; and the Clinical Research Committee of the Middlesex Hospital for a personal research grant (to J. D. N. N.).

ADDENDUM.—Since this report was written the one patient who was responding poorly has developed a severe neutropenia. After ten weeks' treatment in which the dose ranged from 1 to 2.5 g. a day (total amount given 123 g.) she was found to have a white-cell count of 2,100 per c.mm. with only 10% polymorphonuclear leucocytes. There was a mild fever at this time which responded to penicillin. She has now been off the tablets for two weeks and the blood count shows 5,700 white cells per c.mm. with 33% neutrophils.

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THE VALUE OF BZ 55 IN CONTROL OF DIABETES

BY

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It has been reported that BZ 55 is capable of controlling the glycosuria of a middle-aged obese diabetic, but that it is ineffective in the young acute thin type of individual, the type which generally requires insulin, without which ketosis is very apt to occur. The obese diabetic in this country is generally treated by dietary restriction alone, and excellent results are commonly obtained as the weight is reduced to the "ideal." Nevertheless, one encounters from time to time the patient who has brought down the weight to the desired level, and who, although often devoid of diabetic symptoms, still shows hyperglycaemia and glycosuria, which eventually calls for the administration of insulin. Such patients would appear to be the type ideal for testing the efficacy of BZ 55. Bertram *et al.* (1955) concluded that success with this preparation was most likely to be obtained in the patient developing diabetes after the age of 45, who had not suffered from the disease for more than 10 years, and who, if treated with insulin, had not taken this for a period exceeding two years.

Accordingly, for the purpose of our investigation into the efficacy of BZ 55 in controlling hyperglycaemia and glycosuria we selected 23 patients who were over 45 years of age at the time of onset of the disease and who were now approximately the "ideal" weight. Of these 23 patients, 12 had formerly been obese (more than 20% above ideal weight), and 9 of these 12 had never received insulin. Another 11 patients had never been overweight, and eight of these had never had insulin. At the start of the trial no patient had ketonuria, but this had been noted at some time previously in seven patients, in three of whom this had been of considerable degree. In addition to these 23 patients, two younger diabetics were included in this study: one, who had recently developed the disease, in the hope that with the use of this preparation insulin might be avoided; the other, an unstable diabetic, to discover whether the insulin requirements might be reduced. The age and sex of the patients and the duration of diabetes are shown in Table I.

TABLE I

Type	Male	Female	Age (Years)	Duration of Diabetes		
				<1 Year	<10 Years	>10 Years
Previously obese	4	8	56–79	3	4	5
Never overweight	4	7	50–70	3	6	2
Young	0	2	19–30	1	1	—

Methods

As many of the patients were devoid of symptoms it was thought unjustifiable to admit these to hospital for the purpose of this investigation, and a large proportion of our cases were studied as out-patients. They were all familiar with their prescribed diet, which provided, in measured quantities, adequate carbohydrate to satisfy their require-

ments. With such a diet the co-operation of patients is usually not difficult to obtain, particularly when they know that they are taking part in a study of this nature. However, for the first two weeks they were given dummy tablets ("A" tablets), and thereafter they had, for a further course of two weeks, tablets of similar appearance but each containing 0.5 g. of BZ 55 ("B" tablets). In each case the initial dose was five tablets, reduced to three on the second day, and thereafter two daily were taken. Blood-sugar estimations were done at noon on the 4th, 7th, 11th, and 14th days of each course. During the last six days of each course, 24-hour collections of urine were made, in each of which the amount of sugar and of creatinine, the latter as a check on the accuracy of the collection, was determined. With in-patients a similar procedure was adopted, but the control period on dummy tablets was restricted to six days, and throughout this time and the subsequent course of B tablets, daily blood-sugar and urine-glucose estimations were carried out.

Results

The results obtained in this trial of BZ 55 have been classified according to the degree of success. Those patients in whom the mean blood sugar at noon was reduced to less than 180 mg. per 100 ml. and who showed marked improvement in the urinary output of glucose were regarded as "successes." When the glycosuria was greatly lessened, although the noon blood sugar was relatively little affected and was above 180 mg. per 100 ml., the result was classified as a "partial success." The results obtained from the study of the 23 patients aged over 45 are summarized in Table II.

TABLE II

Result	No. of Cases	Previous Build		Previously Taking Insulin	Mean Noon Blood Sugar (mg./100 ml.)		Daily Urinary Glucose (g.)	
		Obese	Non-obese		"A" Tabs.	"B" Tabs.	"A" Tabs.	"B" Tabs.
Success ..	11	4	7	0	230	145	29	5
Partial success	6	5	1	1	276	227	49	12
Failure ..	6	3	3	6	282	262	48	61

It will be observed that 11 of these patients showed a completely satisfactory response. In some cases this was dramatic, the glycosuria virtually disappearing within 24 hours of the initial dose. It is noteworthy that none of these patients had ever received insulin, although, particularly in the case of the seven who had never exceeded the ideal weight, insulin treatment might well have become necessary.

The response to treatment with BZ 55 of the group classed as "partial success" was unsatisfactory, and, despite the quite appreciable reduction of glycosuria, these cases should probably be regarded as failures. Certainly the blood sugar, even if lowered in some instances, remained at an undesirably high level, and it is significant that four of the six cases showing this type of response are now getting insulin, and this will probably be required by the remaining two. Attention should be drawn to the fact that all of the group of six unquestionable failures had previously received insulin, although half of them had had this for less than two years. Sex and age distribution and duration of diabetes were similar in all three groups, and did not appear to account for differences in response to the drug.

One factor which appeared to militate against a satisfactory response to BZ 55 was the presence of sepsis. One patient who had a severe infection in the urinary tract failed to show any improvement with the drug, but after recovery from this the trial was repeated and the response was found to be excellent, the blood sugar averaging 150 mg. per 100 ml., and glycosuria became minimal. In another case with considerable sepsis of a leg, no response was obtained when BZ 55 was given at an initial trial, but after the sepsis had cleared up the mean blood sugar, with a subsequent trial, fell from 276 to 204 mg. per 100 ml., and urinary sugar from 22.6 to 7.2 g. a day, and so was classified as a partial success.

A history of severe ketonuria in the past may be of significance. As mentioned above, this had been noted in three patients in this series. All of these failed to show any response to treatment with BZ 55.

The two younger patients to whom BZ 55 was given failed to show any improvement. In one who was a very unstable diabetic the drug did not diminish the insulin requirements. The other patient, a woman aged 30, had been diabetic for only two months, and, having heard of an oral remedy, was opposed to taking insulin; she showed no improvement in either blood-sugar level or urinary glucose output with BZ 55.

In no case was there any manifestation of toxic effects as a result of the administration of BZ 55.

Discussion

The results given above confirm previous reports that BZ 55 is efficacious in controlling the hyperglycaemia and glycosuria in certain diabetic patients. It is important to discover the type of case that might be expected to show a satisfactory response, but it is equally important to know whether the administration of this preparation might be fraught with danger. It has been suggested that observation of blood-sugar levels for four hours after a test dose of 4 g. of BZ 55 will show whether or not a patient is likely to derive benefit from the drug. We have tried this test in a number of patients, but our results have been equivocal, and more experience with the test is necessary before it can be relied on for this purpose. The definition given by Bertram *et al.* (1955) of the type to be considered suitable for treatment with BZ 55 is not quite adequate. Four of our patients who responded well had been diabetic for much longer than 10 years, while three of the failures had received insulin for less than two years. One would agree, however, that it is the older patient, over 45 years of age, who is most likely to respond.

Our results suggest, although the number of our cases is small, that a patient is more likely to benefit if never previously treated with insulin. Patients taking insulin might, of course, be regarded as more severe cases, and their failure to respond to treatment with BZ 55 attributed to this, but Bertram *et al.* (1955) reported that response to the drug was independent of the severity of the disease. The size of dose of insulin does not appear to be a criterion, as we had one patient, previously well controlled with only 16 units of insulin zinc suspension, who rapidly developed ketonuria and heavy glycosuria on stopping this and transferring to BZ 55. Moreover, when insulin is required we have not found that BZ 55, given in addition, has any insulin-sparing effect.

At the present time it appears that this preparation may be of value in the treatment of elderly diabetics who, if they have been obese, still show glycosuria after reduction to "ideal" weight, or those who, although never overweight and have never had ketonuria, are still uncontrolled by diet. It is unsuitable for the younger acute diabetic, who may rapidly develop ketosis if insulin is abandoned in favour of BZ 55.

Summary

A trial of BZ 55 in 25 diabetic patients is reported. In 23 patients, all over age 45 when they developed diabetes, and all approximating to the "ideal" weight, very successful control of hyperglycaemia and glycosuria was obtained in 11. The remaining 12 patients failed to respond satisfactorily. In two younger patients the drug proved completely ineffective.

BZ 55 proved ineffective in two patients while they were suffering from sepsis, but produced considerable effect when this was overcome.

No satisfactory explanation is given for success or failure with this drug, but it is pointed out that all patients in this series who showed no response had previously received insulin.

Ketosis may develop rapidly on the substitution of insulin by BZ 55 in patients who require the former for their control.

We wish to acknowledge our indebtedness and thanks to Mr. A. P. Kenny, of the Biochemical Department, Victoria Infirmary, Glasgow, for undertaking the blood-sugar and urine-sugar estimations, and to British Insulin Manufacturers, who kindly provided us with the A and B tablets.

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A WARNING NOTE

In view of a recent report from America of a small number of cases of severe agranulocytosis and also of several cases of thrombocytopenia in this country, it is the considered opinion of the authors of the papers on BZ 55 appearing in this issue of the "British Medical Journal" that the drug in question should at present be used only under careful hospital supervision.

This view is shared by the majority of those who have had experimental and clinical experience of the use of BZ 55 in this country.

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J. D. N. NABARRO, Middlesex Hospital.
W. G. OAKLEY, King's College Hospital.
F. W. WOLFF, the Wellcome Research Institute.

VACCINATION AGAINST WHOOPING-COUGH

RELATION BETWEEN PROTECTION IN CHILDREN AND RESULTS OF LABORATORY TESTS

A REPORT TO THE WHOOPING-COUGH IMMUNIZATION COMMITTEE OF THE MEDICAL RESEARCH COUNCIL AND TO THE MEDICAL OFFICERS OF HEALTH FOR CARDIFF, LEEDS, LEYTON, MANCHESTER, MIDDLESEX, OXFORD, POOLE, TOTTENHAM, WALTHAMSTOW, AND WEMBLEY*

In a previous report (Medical Research Council, 1951) the results were given of a series of controlled trials made to assess the prophylactic value of pertussis vaccine in children 6 to 18 months old. Five batches of vaccine from three different manufacturers were tested. Each batch gave substantial protection, but the two batches supplied by the Michigan Department of Health gave much greater protection than the others.

In 1948, before the previous trials were completed, further field investigations were begun in conjunction with laboratory studies to determine whether the protective effect of vaccines in children could be assessed by a laboratory test. Two series of trials were made—one from October, 1948, to March, 1951, using British vaccines, and the other from early 1951 to mid-1954, using British and American vaccines. The second series was planned not only to give information on the relation between field and laboratory results, but also to determine whether British manufacturers could produce good vaccines by methods similar to those of the Michigan Department of Health and to determine whether a vaccine prepared from culture in liquid medium was as effective as one from culture on solid medium. A description of all the vaccines used in the two series of trials is given in Table I.

INVESTIGATIONS IN THE FIELD

General Plan

The previous trials (M.R.C., 1951) were made on a strictly controlled basis to investigate whether pertussis vaccines were of any value in protecting against the disease. Half the children whose parents volunteered to have them injected were given vaccine and the rest were given injections of an inoculum which looked like pertussis vaccine but which did not contain *Haemophilus pertussis*. This procedure could not be continued after it was known that each of five different batches of vaccine used gave substantial protection, and it was decided that in all subsequent trials every child should be given pertussis vaccine, and that the results with one batch of vaccine should be compared with those with other

**Whooping-cough Immunization Committee:* Sir Samuel Bedson, F.R.S. (chairman), Dr. P. Armitage, Dr. W. C. Cockburn, Dr. E. T. Conybeare, Professor R. Cruickshank, Professor A. W. Downie, F.R.S., Professor A. Bradford Hill, F.R.S., Dr. J. O. Irwin, Dr. Pearl Kendrick, Dr. J. Knowelden, Professor J. W. McLeod, F.R.S., Dr. H. J. Parish, Mr. A. F. B. Standfast, Dr. G. S. Wilson, Dr. J. Ungar, Dr. D. G. Evans (secretary).

Medical Officers of Health: Dr. J. Greenwood Wilson and Dr. W. Powell Phillips, Cardiff; Dr. I. G. Davies, Leeds; Dr. A. W. Forrest, Leyton; Dr. C. Metcalfe Brown, Manchester; Dr. A. C. T. Perkins, Middlesex; Dr. J. F. Warin, Oxford; Dr. G. Chesney and Dr. J. Hutton, Poole; Dr. G. Hamilton Hogben, Tottenham; Dr. A. T. W. Powell, Walthamstow; Dr. E. Grundy, Wembley.

Field Workers: Dr. I. A. Bolz and Miss M. R. Elliott, Cardiff; Dr. G. R. Baxter and Mrs. E. R. Beard, Leeds; Dr. A. R. Fox and Miss R. M. Edward, Leyton; Dr. B. J. Griffiths and Miss O. I. Howell, Manchester; Dr. Beryl Anscombe, Dr. A. M.-M. Payne, and Miss C. H. Rudkin, Oxford; Dr. Joan Moignard, Miss M. D. Smith, and Miss W. E. Bennett, Poole; Dr. A. T. W. Powell and Mrs. H. M. Johnston, Walthamstow; Dr. J. C. McDonald, Miss M. M. Wall, and Miss E. E. Wilden, Tottenham and Wembley.

Laboratory diagnostic tests were made by: Dr. G. J. G. King and Mr. E. C. Young, Bournemouth; Dr. J. Marks and Professor Scott Thomson, Cardiff; Dr. H. D. Holt, Mr. G. V. Heimer, and Mr. J. Hollingsworth, Colindale; Professor J. W. McLeod, F.R.S., Dr. D. E. Nicholson, Dr. G. C. Turner, and Miss B. B. Waller, Leeds; Dr. W. W. Walther and Mr. K. R. Podger, Leyton; Dr. Mary O. Adams and Mr. A. G. Harbour, Manchester; Dr. W. H. H. Jebb, Oxford; Dr. F. Marsh, Mr. E. F. Browning, Mr. P. Lovell, and Mr. G. Hoy, Walthamstow.

Laboratory tests for antigenic potency were made by: Mr. A. F. B. Standfast, Lister Institute; Dr. Margaret Pittman, U.S. National Institutes of Health, Bethesda; Dr. Pearl Kendrick and Dr. Grace Eldering, Michigan Department of Health; Dr. A. E. Francis and Mr. H. Proom, Wellcome Research Laboratories; Dr. D. G. Evans and Dr. F. T. Perkins, M.R.C. Laboratories; Hampstead; Dr. J. Ungar, Glaxo Research Laboratories, Dr. Mary O. Adams, Manchester; Dr. Naomi Datta, Colindale.

The field trials were put in train and supervised by Dr. W. C. Cockburn.

The analysis of the field and laboratory results were made and the report prepared by Dr. P. Armitage, Dr. W. C. Cockburn, Dr. D. G. Evans, Dr. J. O. Irwin, Dr. J. Knowelden, and Mr. A. F. B. Standfast.

batches tested at the same time in the same area. There were therefore no unvaccinated control groups, but in some of the trials records were kept of the incidence of pertussis in the siblings of vaccinated children when the vaccinated children and the siblings were known to be exposed to infection by a primary case in the family. This was the main difference between the new and the earlier studies; otherwise the procedure in the field was similar to that described in the 1951 Report.

Children in the 1948–51 trials were allocated to a vaccine group in succession as their names were received. In the 1951–4 trials, when only two vaccines were tested in each area at one time, children born on *odd* days of the month were allocated to one group and children born on *even* days to the other. After the injections had been completed, arrangements were made for each child to be visited monthly for about 24 months. Special visits were paid when it was known that a child was being exposed to pertussis or had symptoms which might be those of the early stages of the disease. Swabs were taken from vaccinated children with coughs and also so far as possible from infective cases to which vaccinated children were exposed. The doctors and nurse-investigators visiting children during the follow-up period did not know which vaccine a child had received.

Trials Made Between 1948 and 1951

Seven separate trials were made in six areas—Cardiff, Leyton, Manchester, Oxford, Poole, and Walthamstow; two were made in Manchester and one in each of the other areas. The vaccines used—V1, V2, V3, V3b, V4, V5, V5a, V6, and V7—were prepared by different methods from the same strains of *H. pertussis* (Table I). In each trial three vaccines were tested in parallel. Vaccines V1, V2, and V3 were tested in Cardiff, Poole, Leyton, and Walthamstow, vaccines V3b, V4, V5a, V5, V6, and V7 in Manchester, and vaccines V2, V3b, and V4 in Oxford.

Children 6–18 months old were given three doses of vaccine intramuscularly with an interval of one month between injections. The first two doses were each 0.5 ml., the third 1 ml., and the total dose, in terms of the U.S.A. opacity standard, was approximately 70,000 million organisms. Consent forms were received from the parents of 11,093 children in all areas; 9,794 (88%) of the children completed the course of three injections.

Reactions and Untoward Sequelae

In the trials with plain suspension vaccines—V1, V2, and V3—940 children, about 20% of the total, were visited 24–48 hours after each injection, and degrees of redness, swelling, and general malaise, and other reactions were estimated. According to the trial area, one-half to one-third of the children had no local or general reaction. Of those who had reactions, all but nine had mild malaise of 24–48 hours or redness or swelling about an inch (2.5 cm.) in diameter. Three of the nine children with more serious reactions had malaise severe enough for them to be kept in bed for 24–48 hours and six had screaming attacks in the evening of the day of injection; between the screaming attacks the children were said to be pale and limp. These episodes were not confined to any one of the three injections; some occurred after the first, some after the second, and some after the third. Three of the nine children were given subsequent injections without ill effect. In the Manchester trial with the alum-precipitated vaccines V3b, V4, and V5a, 194

TABLE I.—*Vaccines and Dosage Schedule*

Vaccines									Dosage Schedule	
Batch No.	Date of Prep.	Medium for Growth	Killing Agent and Concentration	Alum-precipitated or Plain	Preservative and Concentration	Strains of *H. pertussis*	Other Details of Preparation	No. of Organisms (Millions/ml.)	Doses at Monthly Intervals (ml.)	Total Dose in Millions of Organism
V1	Sept., 1948	BG with horse blood	Formalin 0·5%	Plain	Phenol 0·5%	2128	48-hr. growth	35,000	0·5, 0·5, 1	70,000
V2	,, ,,	,, ,,	,,	,,	,, ,,	2128	Similar method to V1	35,000	0·5, 0·5, 1	70,000
V3	,, ,,	,, ,,	,,	,,	Thiomersalate 0·01%	2128	24-hr. growth	35,000	0·5, 0·5, 1	70,000
V3b	,, ,,	,, ,,	,,	Alum pptd.	,,	2128	Same batch as V3 but alum pptd.	35,000	0·5, 0·5, 1	70,000
V4	July, 1948	Cohen and Wheeler	,,	,, ,,	,,	2128	Whole fluid from 20-hr. growth; culture shaken	35,000	0·5, 0·5, 1	70,000
V5	April, 1949	BG with horse blood	,,	,, ,,	Phenol 0·5%	2128	Same method as for V1 but alum pptd.	35,000	0·5, 0·5, 1	70,000
V5a	Oct., 1948	,, ,,	,,	,, ,,	,, ,,	2128	,, ,,	35,000	0·5, 0·5, 1	70,000
V6	April, 1949	,, ,,	,,	,, ,,	Thiomersalate 0·01%	2128	Same method as for V3 but alum pptd.	35,000	0·5, 0·5, 1	70,000
V7	Mar., 1949	Cohen and Wheeler	,,	,, ,,	,,	2128	Same method as for V4	35,000	0·5, 0·5, 1	70,000
V8	Dec., 1949	BG with sheep blood	Thiomersalate 0·01%	Plain	,,	18925; 16945; 10536; 18334	Michigan method	20,000	1 1 1	60,000
V9	June, 1950	,, ,,	,,	,,	,,	83E; 252; L46; C26573; 2891; 2893	,, ,,	20,000	1 1 1	60,000
V10	Nov., 1950	,, ,,	,,	,,	,,	83E; 252; L46; C26573; 2891; 2893	,, ,,	20,000	1 1 1	60,000
V11	Aug., 1950	Cohen and Wheeler	,,	,,	,,	18925; 16945; 10536; 18334	Whole fluid from 72-hr. growth; culture not shaken	30,000	1 1 1	90,000
V12	Sept., 1951	BG with human blood	Thiomersalate 0·02%	,,	Thiomersalate 0·013%	293; 324; 360; 357; 358; 332; 343	Michigan method but with human blood in BG	20,000	1 1 1	60,000

BG = Bordet–Gengou medium.

TABLE II.—1948–51 *Trials. Similarity of Groups*

	Areas and Vaccines											
	Cardiff, Poole, Leyton, Walthamstow			Manchester			Manchester			Oxford		
	V1	V2	V3	V3b	V4	V5a	V5	V6	V7	V2	V3b	V4
No. of children followed up ..	1,709	1,701	1,648	910	943	941	414	396	417	230	241	244
Percentage of males	50	50	51	52	51	51	54	54	51	53	55	54
Average age (months)	13	13	13	15	15	14	15	15	15	14	14	14
Average duration of observation per child (months)	20	20	20	27	27	27	23	23	22	25	25	25
Infectious diseases* during follow-up:												
Total No. of illnesses	644	584	629	483	528	492	161	139	151	71	126	84
Average No. of illnesses per child	0·38	0·34	0·38	0·53	0·56	0·52	0·39	0·35	0·36	0·31	0·52	0·34
Average No. of other children per household under 14 years of age	0·93	0·93	0·98	0·76	0·84	0·77	0·89	0·85	0·90	0·99	1·15	0·98

* Measles, chicken-pox, mumps, rubella.

children, 7% of those followed up, were similarly visited after each injection. One severe reaction was noted, in a child who developed extensive redness and swelling after the third injection.

Particular attention was paid to the occurrence of convulsions in all children vaccinated in all areas. Four children had convulsions within 72 hours after an injection. One of these children was given a subsequent injection without ill effect. None of the children showed evidence of permanent cerebral damage.

None of the children developed poliomyelitis within four weeks after injection.

Similarity of Groups

To determine whether the vaccine groups in each trial were essentially alike certain attributes were examined. Table II records the results of the tests for similarity; it is clear that with each set of three vaccines the groups were similar.

TABLE III.—1948–51 *Trials. Number of Cases of Pertussis and Attack Rates per* 1,000 *Child-months of Observation*

Area	Vaccine	No. Followed Up	Duration of Observation (Child-months)	Cases of Pertussis	Attack Rate per 1,000 Child-months
Cardiff ..	V1	1,709	34,850	247	7·1
Poole ..	V2	1,701	34,359	276	8·0
Leyton ..	V3	1,648	33,234	190	5·7
Walthamstow					
	V3b	910	25,002	101	4·0
Manchester	V4	943	25,692	164	6·4
	V5a	941	25,667	112	4·4
	V5	414	9,420	35	3·7
.. ..	V6	396	9,003	36	4·0
	V7	417	9,304	37	4·0
	V2	230	5,741	55	9·6
Oxford ..	V3b	241	6,023	28	4·6
	V4	244	6,143	44	7·2
Totals		9,794	224,438	1,325	5·9

Incidence of Pertussis

The results of all trials are given in Tables III and IV. Altogether 1,325 cases of pertussis were diagnosed, and in 68% the diagnosis was confirmed bacteriologically. By all three methods of comparing the vaccines—the attack rate per 1,000 child-months (Table III) and the percentage attack rates for "home exposures" and "other exposures" (Table IV)—no striking differences in protective effect were seen. Some slight differences did, however, exist, and these are referred to later.

Since there were no unvaccinated control groups in these trials, an absolute estimate of the value of the vaccines could not strictly be made. In the previous trials (M.R.C., 1951) the attack rate in "home exposures" in the unvaccinated control groups was 87%. Similar high attack rates in susceptible children exposed in their own homes have been reported by others (Wheeler, 1936; Kendrick and Eldering, 1939; Court *et al.*, 1953). In the present study, taking all vaccines together, 547 children were exposed in their own homes; of these, 379 (69%) developed the disease. This attack rate is much nearer the 87% in the unvaccinated than the 18% in the vaccinated groups in the previous study. Furthermore, only one vaccine, V3b in the Oxford trial, gave a home exposure attack rate of less than 50%, and this was based on only 18 home exposures (Table IV). All the vaccines in this new series of trials were therefore poor.

Trials Made Between 1951 and 1954

11 trials were made in this series, in Cardiff, Leeds, Manchester, Oxford, Poole, Tottenham, and Wembley (Tottenham and Wembley were considered as a combined area). The Michigan Department of Health provided a vaccine—V8—in

TABLE IV.—1948–51 *Trials. Number of Cases of Pertussis and Percentage Attack Rates by Type of Exposure*

Area	Vaccine	Home Exposures			Other Exposures			No. of Cases After No Known Exposure	Total Cases
		No. of Exposures	No. of Cases	Attack Rate (%)	No. of Exposures	No. of Cases	Attack Rate (%)		
Cardiff ..	V1	93	73	78	197	62	31	112	247
Poole ..	V2	88	75	85	203	57	28	144	276
Leyton ..	V3	109	66	61	216	46	21	78	190
Walthamstow									
	V3b	47	28	60	178	31	17	42	101
Manchester	V4	54	42	78	184	51	28	71	164
	V5a	51	31	61	190	35	18	46	112
	V5	18	11	61	44	10	23	14	35
..	V6	24	12	57	40	10	25	14	36
	V7	16	9	56	42	11	26	17	37
	V2	14	14	100	31	13	42	28	55
Oxford ..	V3b	18	7	39	70	6	9	15	28
	V4	18	11	61	76	10	13	23	44
Totals		547	379	69	1,491	342	23	604	1,325

sufficient quantity for it to be used as a reference vaccine against which the other vaccines could be compared. In each trial half the children were given the reference vaccine V8 and the remainder were given either one of three British vaccines—V9, V10, or V12—made by methods similar to those used by the Michigan Department of Health, or vaccine V11, which was prepared by the State of New York Department of Health from liquid medium culture (Cohen and Wheeler, 1946) using the same strains of *H. pertussis* as were used in the preparation of V8 (Table I). In each area except Oxford, two trials were made. Each vaccine except V9 was tested in parallel against V8 in two areas; V9 was tested against V8 in all areas except Oxford (Table V).

In all the areas the parents of 36,811 children 6 months to 3 years old agreed to have them vaccinated. Three intramuscular or subcutaneous injections were given at monthly intervals. Each dose was 1 ml., and the total dose consisted of 60,000 million organisms (U.S.A. opacity standard). Because of reports that convulsions might occasionally occur after pertussis vaccine, particularly in children with a personal or family history of convulsions or epilepsy, children with such a history were not vaccinated, and on account of this 1,601 children were not accepted. In addition, 2,108 children failed to arrive at the clinics for the first injections. Of the 33,102 who had their first injection, 31,557 (95%) completed the course.

When the trials began it was not known how many children might be presented for vaccination, as vaccination was becoming popular in the trial areas, and hence there was some difficulty in deciding whether all or only a portion of the children could be followed up. At first it was thought that it might suffice to follow only vaccinated children in families where there was also an unvaccinated child with no history of pertussis, such potential "home exposure" families being the ones from which it was known by experience that the most accurate information could be obtained. However, the proportion of children from such families was not more than 10%, and to avoid jeopardizing the studies by having too few children under observation it was decided to increase the numbers taken into the follow-up. After the first few weeks of the trial, approximately all the children were followed up in Cardiff, Oxford, Poole, Tottenham, and Wembley, and approximately half the children in Leeds and Manchester. The total number of children followed up was 19,005. In the areas where half the children were followed up, every second child presented for vaccination was chosen, and the others, though not followed up, were given a full course of vaccine.

Reactions and Untoward Sequelae

Local and General

One child in five from the follow-up groups was visited 48 hours after each injection to determine the incidence of local and general reactions. Children chosen for visiting after the first injection were also visited after the second and third injections. Nearly 10,500 visits were made. There was considerable variation in recording between areas, presumably due to observer differences, but very little difference within areas between vaccines and between the first, second, and third dose. Redness more than 2 in. (5 cm.) in diameter was noted on 6% of visits (not of children) and the child appeared "obviously disturbed by the tenderness" on 0.4% of visits. Other reactions noted were that three children were kept in bed for more than 24 hours, 99 vomited once or oftener within 48 hours after an injection, and 72 were described as "fretful," "didn't sleep," or "had lost their appetites." Local and general reactions were therefore not serious.

Convulsions

As in the 1948–51 series of trials, special notes were kept of children who developed convulsions after vaccination. Children not in the follow-up were visited after the first and second injections if they failed to return to the clinic for the next injection, and convulsions in these children were recorded if they occurred. The children not in the follow-up, however, were not visited after the third injection. All children known to have had convulsions, whether or not in the follow-up group, were visited at intervals until May, 1955.

A report by Byers and Moll (1948) indicated that in cases of encephalopathy associated with vaccination the first convulsion occurred within 72 hours after an injection. In this series of trials eight children had their first recorded convulsion within 72 hours after one of the three injections. It is impossible to say whether or not the number of cases observed was greater or less than might be expected to occur by chance in this period. Thirty-four children had their first recorded convulsion 4 to 28 days after injection. There is no reason to consider their convulsions were precipitated by the vaccine. Of them, 11 (32%) had more than one convulsion during the period of observation. Of the eight children who had convulsions within 72 hours after injection, three (38%) had more than one attack. The proportions of the two groups are similar and, though based on small numbers, suggest that serious cerebral damage, as manifested by repeated convulsions, did not occur as a result of the injections. None of the children with repeated convulsions showed evidence of gross cerebral damage such as was noted by Byers and Moll, but one child had five convulsions during the period of observation and two had four. These three children had their initial convulsions 12, 17, and 20 days after injection.

In over 30,000 vaccinated children, therefore, there was no definite evidence that convulsions or encephalopathy were directly related to vaccination. As previously stated, children with a personal or family history (the family for the purpose was taken to include only father, mother, sisters, and brothers) of convulsions, epilepsy, hydrocephalus, mental defect, or similar conditions were not accepted in the trial. In addition, children were not injected within a month after attacks of measles, mumps, influenza, chicken-pox, and similar diseases, or smallpox vaccination. These precautions may account for the freedom from cerebral accidents, but it may also be that the risk of

TABLE V.—1951–4 *Trials. Similarity of Groups*

	Areas and Vaccines							
	All Except Oxford		Leeds, Tottenham, Wembley		Oxford, Poole		Cardiff, Manchester	
	V8	V9	V8	V10	V8	V11	V8	V12
No. of children followed up	3,342	2,975	2,397	2,311	1,254	1,195	2,835	2,696
Percentage of males	51	51	51	54	52	49	53	52
Average age (months)	22	21	18	18	15	16	17	17
Average duration of observation per child (months)	25	25	22	22	22	23	22	22
Infectious diseases* during follow-up: Total No. of illnesses	892	795	372	392	108	115	345	301
Average No. of illnesses per child	0·27	0·27	0·16	0·17	0·09	0·10	0·19	0·19
Percentage of children with previous history of measles	18	20	8	8	4	5	10	9
Average No. of other children per household under 14 years of age	1·1	1·2	0·92	0·93	0·83	0·92	1·2	1·2

* Measles, chicken-pox, mumps, rubella.

encephalopathy is so remote that a group of over 30,000 children was not large enough to show that it existed.

Poliomyelitis

Twenty-four children developed paralytic poliomyelitis during the study. Three children became ill less than 28 days after an injection, and all three were paralysed in the injected limb and nowhere else. Twenty-one children became ill 29 days to 26 months after injection. Five had paralysis only in the injected limb, six had paralysis in the injected limb as well as at other sites, and in 13 there was no association between the site of paralysis and the site of injection. The fact that the three children who developed poliomyelitis within a month after injection had paralysis only in the injected limb suggests, in view of the published evidence, that there was a causal relationship between the injection and the site of paralysis.

Similarity of Groups

In each trial there were two groups of children, those given the reference vaccine V8, and those the vaccine under test. In Table V trials made in the different areas with the same pair of vaccines are combined; it is clear that with each pair of vaccines the groups were similar in all respects for which information was obtained. In each separate trial also the groups were similar.

Incidence of Pertussis

The results of the trials are given in summary form in Tables VI and VII. Altogether 231 children were diagnosed as cases of pertussis, and 59% of these were confirmed bacteriologically. Bacteriological evidence of exposure to infection was also obtained in many cases. Of the 801 vaccinated children exposed in their own homes to infection, *H. pertussis* was isolated from the sibling—or siblings—to whom the vaccinated child was exposed in 64%. Of the 1,967 "other exposures," *H. pertussis* was isolated from the infecting child in 43%.

When chloramphenicol was introduced for the treatment of pertussis it was thought that, if it lessened the period during which infection was dispersed by cases, and was used for the treatment of siblings to whom vaccinated children were exposed, it might reduce the home exposure attack rate and make it impossible to compare rates in the pre- and post-chloramphenicol periods. Records were kept of the use of chloramphenicol in the siblings of vaccinated children. It was found that the attack rate in 128 vaccinated children exposed to chloramphenicol-treated siblings with pertussis was 20% and that the attack rate in 673 vaccinated children exposed to infection by siblings not treated with chloramphenicol was 13%. Thus the use of chloramphenicol for the siblings of vaccinated children did not reduce the risks of the vaccinated children developing the disease.

By all three methods of comparing the vaccines—attack rate per 1,000 child-months (Table VI) and percentage attack rates in "home exposures" and "other exposures" (Table VII)—no outstanding differences in protective effect were evident. The test vaccines were of the same order of potency as the Michigan reference vaccine.

As mentioned earlier, the studies were made to compare vaccines and not to ascertain their absolute value. Some information on absolute values can, however, be deduced. Taking all vaccines together, the attack rate in 801 home exposures was 14%, ranging from 4 to 29% (Table VII). In the controlled trials reported previously (M.R.C., 1951) the attack rate in the control unvaccinated groups was 87%. The evidence, along with the previously mentioned observations of Wheeler (1936), Kendrick and Eldering (1939), and Court *et al.* (1953), suggests that the vaccines used in the 1951–4 series of trials were highly potent unless the disease had recently changed its character and had become less infectious. There is evidence that such a change had not occurred. In the course of the trials there were 56 households in the three largest trial areas—Manchester, Leeds, and Cardiff—in which vaccinated children and unvaccinated children up to 7 years of age were exposed to infection from another case in the family and in which the size of the family at the time of exposure was accurately known.

In the 56 households there were 69 vaccinated and 62 unvaccinated children. Fourteen (20%) of the vaccinated developed pertussis compared with 51 (82%) of the unvaccinated. The diagnosis of pertussis was confirmed bacteriologically in eight (57%) of the vaccinated, in 37 (73%) of the unvaccinated, and in 34 (61%) of the initial cases providing the sources of infection in the households. Eleven per cent. of the vaccinated were under 1 year of age compared with 29% of the unvaccinated, and 16% of the vaccinated were 4 years old or more compared with 48% of the unvaccinated. These differences were mainly due to the ages at which vaccination was offered (6 months to 3 years).

TABLE VI.—1951–4 *Trials. Number of Cases of Pertussis and Attack Rates per 1,000 Child-months of Observation in Areas Testing the Same Two Vaccines*

Area	Vaccine	No. Followed Up	Duration of Observation (Child-months)	Cases of Pertussis	Attack Rate per 1,000 Child-months
Cardiff, Leeds, Manchester, Poole, Tottenham, Wembley	V8	3,342	84,463	46	**0·54**
	V9	2,975	74,984	29	**0·39**
Leeds, Tottenham, Wembley	V8	2,397	52,907	33	**0·62**
	V10	2,311	50,392	48	**0·95**
Oxford, Poole	V8	1,254	28,025	21	**0·75**
	V11	1,195	27,440	13	**0·47**
Cardiff, Manchester	V8	2,835	63,329	26	**0·41**
	V12	2,696	59,548	15	**0·25**
Totals		19,005	441,088	231	**0·52**

TABLE VII.—1951–4 *Trials. Number of Cases of Pertussis and Percentage Attack Rates by Type of Exposure in Areas Testing the Same Two Vaccines*

Area	Vaccine	Home Exposures			Other Exposures			No. of Cases After No Known Exposure	Total Cases
		No. of Exposures	No. of Cases	Attack Rate (%)	No. of Exposures	No. of Cases	Attack Rate (%)		
Cardiff, Leeds, Manchester, Poole, Wembley, Tottenham	V8	172	24	**14**	409	11	**3**	11	46
	V9	132	17	**13**	352	5	**1**	7	29
Leeds, Tottenham, Wembley	V8	84	17	**20**	181	10	**6**	6	33
	V10	85	25	**29**	172	10	**6**	13	48
Oxford, Poole ..	V8	58	3	**5**	159	7	**4**	11	21
	V11	52	2	**4**	163	4	**2**	7	13
Cardiff, Manchester	V8	114	15	**13**	270	2	**0·7**	9	26
	V12	104	9	**9**	261	1	**0·4**	5	15
Totals		801	112	**14**	1,967	50	**3**	69	231

The groups were exposed to infection at the same time in the same families, and the high attack rate in the unvaccinated is so near the rate one would have expected to find on the basis of previous experience that it is justifiable to suppose that no change had occurred recently in the facility with which pertussis spreads in unprotected susceptible children in families and that the vaccines used were uniformly of high potency.

An analysis was made which showed that during the period of observation there was no waning in the degree of immunity afforded by the vaccines. Taking all the vaccines together, the attack rates in "home exposures" at six-monthly intervals after vaccination showed no evidence of increasing two and a half to three years after vaccination (Table VIII).

TABLE VIII.—1951-4 *Trials. Attack Rates in Home Exposures at Six-monthly Intervals after Vaccination in all Trials*

Period After Third Injection	No. of Exposures	No. of Cases	Attack Rate (%)
0–5 months	218	23	11 } 14
6–11 ,, ...	188	35	19 }
12–17 ,, ...	184	22	12 } 14
18–23 ,, ...	123	20	16 }
24–29 ,, ...	79	12	15 } 14
More than 29 months ..	9	—	0 }

In summary, the field trials showed that the vaccines in the first series were poor and in the second series good.

INVESTIGATIONS IN THE LABORATORY

The Mouse-Protection Test

Tests were made in the laboratory to compare the ability of vaccines to protect mice against experimental *H. pertussis* infection. Two methods were first explored—one in which the level of protection of immunized mice was determined by injecting a challenge dose of *H. pertussis* intracerebrally, and the other in which the challenge dose was given intranasally. It was shown (Standfast, 1954) by testing a number of vaccines in parallel by both methods that the intranasal method did not distinguish between the protective power of the vaccines in mice as well as did the intracerebral method. For this reason it was decided to employ only the intracerebral method.

In all, 18 vaccines were tested; four of those used in the previous field trials—D231, O87860, G61, and G174—and all 14 of those in the present trials. The details of the method are fully described in the W.H.O. Report (1953). Groups of 15 mice were injected intraperitoneally with graded doses of vaccine and challenged intracerebrally 10 to 14 days later with a suspension of virulent *H. pertussis*, strain 18-323. The mice were observed for 14 days after challenge, and from the proportion of deaths occurring in each group the dose of vaccine required to protect 50% of mice (ImD_{50}) was calculated. In each test at least two vaccines were compared, one of which was a reference vaccine, usually G61, V3, or V8.

From preliminary studies it became evident that the errors of the tests were large and that, in spite of standardization of reagents and procedures and the use of mice from an inbred stock, many mice would be needed to detect significant differences in potency between vaccines. Two series of tests were therefore made in which three vaccines, V1, V2, and V3, were tested in parallel on 14 occasions in each of two different laboratories. From the results of these tests it was calculated that it was necessary to test any two vaccines in parallel eight times (720 mice) in order that an apparent twofold potency-ratio between them should be significant ($P=0.05$). As a result of this statistical analysis, which will be published in full elsewhere (Irwin and Standfast, 1956), it was decided to test all vaccines at least eight times in one laboratory (Lister Institute) and as often as possible in other laboratories. Some more recent results in the mouse-protection test suggest that the same degree of precision may often be achieved with a smaller number of mice (Irwin and Standfast, 1956; Ungar and Basil, 1956).

Comparison of Vaccines by the Mouse-Protection Test

The comparison of vaccines was made from the results of 118 assays by Mr. Standfast, 21 Dr. Pittman, 12 by Dr. Ungar, 11 by Mr. Proom, and 2 by Dr. Kendrick. It is convenient to divide the vaccines into three groups according to which of three reference vaccines was normally used as a standard of comparison in the laboratory tests. Group 1 consisted of D231, O87860, G61, and G174 (G61 as the reference vaccine), group 2 consisted of V1, V2, V3, V3b, V4, V5, V5a, V6, and V7 (V3 as the reference vaccine), and group 3 consisted of V8, V9, V10, V11, and V12 (V8 as the reference vaccine).

For each vaccine in each assay, the ImD_{50} was estimated by the Reed–Muench method, or, where this was inapplicable, by a rough probit method, and the analysis was performed on the logarithms of the ImD_{50} values. The relative potency of each vaccine in terms of the appropriate reference vaccine was calculated entirely from comparisons made on the same day, since the ImD_{50} has been observed to fluctuate markedly from one day to another. The estimates of the log potency-ratios, with their standard errors, are shown in Table IX. The results from the different laboratories were consistent with each other, and have been pooled. The relative potencies of the three reference vaccines were obtained in the same way, and, finally, each of the 18 vaccines is compared with the vaccine G61. These relative potencies are given in the last two columns of Table IX.

TABLE IX.—*Relative Potencies of Vaccines by Mouse-protection Test*

Vaccine	Log Potency-ratios (±Standard Errors) in Terms of Reference Vaccine			In Terms of G61	
	G61	V3	V8	Log Potency-Ratio	Potency-ratio
Group 1:					
D231	0·594±0·146			0·594	3·93
O87860	0·300±0·219			0·300	2·00
G61 (ref.)	—			0	1·00
G174	−0·944±0·155			−0·944	0·11
Group 2:					
V4 ..		0·365±0·155		0·030	1·07
V7 ..		0·347±0·180		0·012	1·03
V3b ..		0·290±0·167		−0·045	0·90
V6 ..		0·240±0·179		−0·095	0·80
V5a ..		0·176±0·158		−0·159	0·69
V3 (ref.)	−0·335±0·120	—		−0·335	0·46
V5 ..		−0·140±0·180		−0·475	0·34
V1 ..		−0·494±0·062		−0·829	0·15
V2 ..		−1·169±0·098		−1·504	0·03
Group 3:					
V11 ..			0·172±0·095	1·023	10·55
V9 ..			0·107±0·066	0·958	9·08
V12 ..			0·077±0·071	0·928	8·47
V8 (ref.)	0·851±0·129		—	0·851	7·10
V10 ..			−0·269±0·094	0·582	3·82

It should be emphasized that these relative potencies are properties of the vaccines when tested at the same time. For example, V8 is shown as being about seven times as potent as G61. When these two vaccines were tested together, however, V8 was new and G61 was some two to three years old. If each vaccine gradually deteriorated it may be that V8, when new, had about the same potency as G61 when new. In the absence of a standard vaccine known to be stable, the possible deterioration of these vaccines cannot be measured with certainty. However, for almost every vaccine which was tested over a period of more than a year, the ImD_{50} values showed a gradual trend upwards. On the average, this was equal to about 0.2 logarithmic unit a year, equivalent to a loss of potency of 40% per annum. This trend may have been due to a gradual change in the test conditions or to a real deterioration of the vaccines, or both. When comparing the mouse-protection results with those of the field, it has been assumed that the trend was due entirely to deterioration of the vaccines.

The Mouse-Agglutination-Production Test

A number of vaccines were also tested for their ability to produce agglutinin in mice, using the method described by Evans and Perkins (1953, 1954). Groups of mice were given two spaced injections of vaccine separated by an interval of 14 days, and the geometric mean agglutinin titre of the sera was determined 10 days after the second dose. Since the method was introduced late during the field studies, it was not possible to test all vaccines extensively. However, 13 vaccines were tested—one from the previous trials and 12 from the new series. With each vaccine the agglutinin response to a total dose of 10×10^9 organisms was determined, and in the case of five of the vaccines the response to two additional smaller doses, 2.5×10^8 and 0.625×10^8, was also obtained. Each vaccine was tested in parallel with a reference vaccine which gave only a slight variation in response in the different tests. The detailed results have already been reported (Evans and Perkins, 1953, 1954).

A rough comparison of the vaccines may be made from the results shown in Table XII, in which the response obtained with each of the 13 vaccines to a total dose of 10×10^9 organisms is given.

Production of Agglutinin in Children

Tests were made with 13 of the vaccines to determine their ability to produce specific agglutinin in children. Two independent studies were made. In the first, tests were made by Dr. Mary O. Adams on the sera of children immunized with vaccines V1 to V8 and V12. These sera were taken from children aged 6 to 18 months 2 to 10 months after their third inoculation, and the titrations were made using as antigen a suspension of living *H. pertussis* according to the method described by Evans and Adams (1952). In the second study the tests were made by Dr. Naomi Datta on the sera of children immunized with vaccines V8, V10, V11, and V12. These sera were from 2- to 5-year-old children, and were taken 6 to 10 weeks after the third dose of vaccine. The titrations were made by a method similar to that used by Dr. Adams, except that a killed suspension of *H. pertussis* was used as antigen. Similar results were obtained by both workers in testing sera from children immunized with vaccines V8 and V12; more than 90% of the sera with these two vaccines gave titres of 16 or more in both studies. It was therefore considered justifiable to compare the vaccines by grouping the results of all the tests in spite of the fact that the tests had not all been made by a standard method (Table X).

TABLE X.—*Comparison of Vaccines by the Agglutinin Response in Children*

Vaccine	No. of Sera Tested	Sera with Titre of 16 or More		Geometric Mean Titre
		No.	%	
V1	55	2	3·6	4
V2	61	1	1·6	4
V3	52	2	3·8	4
V3b	45	5	11·1	6
V4	39	3	7·7	7
V5	9	0	0·0	4
V5a	30	7	23·3	12
V6	10	1	10·0	5
V7	9	1	11·1	5
V8	267	251	94·0	211
V10	81	73	90·2	208
V11	60	58	96·7	291
V12	126	120	95·2	279

COMPARISON OF FIELD AND LABORATORY TESTS

Field Trials and Mouse-Protection Tests

A comparison of the prophylactic effect of vaccines in the field is most safely made when the vaccines are tested at the same time in the same centres, otherwise the comparison may be distorted by changes in the field conditions or deterioration of the vaccines. These strict comparisons, made on the home-exposure attack rate for reasons given in the first section of this report, are presented in Table XI alongside the corresponding potencies estimated in the laboratory. Differences in either field or laboratory results which are significant at the 0.05 level of probability are also indicated.

Though field and mouse-protection test results occasionally put vaccines in different orders of potency, there are no definite contradictions; on no occasion was a significant

TABLE XI—*Comparisons of Field and Mouse-protection Results for Vaccines Tested in the Field at the Same Time and in the Same Centre*

Vaccine	Results of Field Trials				Results of Mouse-protection Tests	
	Centres	Home Exposures		Significant Differences	Potency in Terms of G61 by Mouse-protection Test	Significant Differences
		Cases/Exposures	Attack Rate (%)			
Group 1:						
D231	Manchester*	2/20	10	None	3·93	None
O8 7860		8/36	22		2·00	
G174	Leeds*	7/29	24	None	0·11	G61 better than G174
G61		7/23	30		1·00	
Group 2:						
V3	Cardiff, Poole, Leyton, Walthamstow	66/109	61	V3 better than either V1 or V2	0·46	V3 better than V1
V1		73/93	78		0·15	V1 better than F2
V2		75/88	85		0·03	
V3b	Manchester	28/47	60	V3b and V5a pooled better than V4	0·90	None
V5a		31/51	61		0·69	
V4		42/54	78		1·07	
V3b	Oxford	7/18	39	V3b and V4 both better than V2	0·90	V3b and V4 both better than V2
V4		11/18	61		1·07	
V2		14/14	100		0·03	
V7	Manchester	9/16	56	None	1·03	None
V6		12/21	57		0·80	
V5		11/18	61		0·34	
Group 3:						
V9	All areas except Oxford	17/132	13	"	9·08	"
V8		24/172	14		7·10	
V8	Leeds, Tottenham, Wembley	17/84	20	"	7·10	V8 better than V10
V10		25/85	29		3·82	
V11	Oxford, Poole	2/52	4	"	10·55	None
V8		3/58	5		7·10	
V12	Cardiff, Manchester	9/104	9	"	8·47	"
V8		15/114	13		7·10	

* These vaccines were not used at the same time, but a large part of the subsequent follow-up periods overlapped.

difference found in one direction in the field and in the opposite direction by the mouse-protection test. Furthermore, in certain comparisons, both field and mouse-protection test results gave significant differences in the same direction. These were: (*a*) that V3 was better than both V1 and V2, and (*b*) that both V3b and V4 were better than V2.

The results of Table XI may be supplemented by a rather less rigorous comparison of the field and mouse-protection test results for all vaccines. Table XII shows, for each vaccine; (*a*) the home-exposure attack rate for all children inoculated with that vaccine, and (*b*) the estimated potency-ratio by the mouse-protection test of the vaccine, at about the middle of the period during which it was used in the field, in comparison with the potency of G61 at the beginning of 1947. The assumption has been made here that each vaccine deteriorated at a rate of 0.2 log unit of potency each year. Thus vaccine V5a was used during a period centred at about the beginning of 1949. Its log-potency-ratio in comparison wth G61 *when tested simultaneously* is given in Table IX as −0.159. We assume that G61 declined in potency by 0.2 log unit during each of the years 1947 and 1948. Then the log-potency-ratio of V5a at the beginning of 1949, in terms of G61 at the beginning of 1947, will be estimated at $-0.159-2(0.2)=-0.56$.

TABLE XII.—*Comparison Between Results of Field Trials and Laboratory Tests*

Vaccine	Results of Field Trials			Results of Laboratory Tests			
	Mean Year* of Inoculation in Children	Home Exposures		Potency by Mouse-protection Test in Terms of G61 in 1947·0		Mean Agglutinin Titre	
		Cases/ Exp.	Attack Rate (%)	Log Ratio	Ratio	In Mice	In Children
V11	1952·3	2/52	4	−0·04	0·91	1,259	291
D231	1947·4	3/41	7	0·51	3·24	1,125	NT
V12	1952·4	9/104	9	−0·15	0·71	1,990	279
V9	1951·5	17/132	13	0·06	1·15	2,820	NT
V8	1952·0	59/428	14	−0·15	0·71	708	211
O87860	1947·1	8/36	22	0·28	1·91	NT	NT
V10	1952·2	25/85	29	−0·48	0·33	644	200
G61	1947·5	7/23	30	−0·10	0·79	NT	NT
G174	1948·7	14/47	30	−1·28	0·05	"	"
V3b	1949·0	35/65	54	−0·44	0·36	"	6
V7	1949·5	9/16	56	−0·49	0·32	16	5
V6	1949·5	12/21	57	−0·60	0·25	49	5
V3	1949·5	66/109	61	−0·89	0·13	13	4
V5	1949·5	11/18	61	−0·98	0·10	14	4
V5a	1949·0	31/51	61	−0·56	0·28	NT	12
V4	1949·0	53/72	74	−0·37	0·43	17	7
V1	1949·5	73/93	78	−1·33	0·05	15	4
V2	1949·5	89/102	87	−2·00	0·01	10	4

* 1952·3 means 0·3 of the way through 1952, and so on.
NT = Not tested.

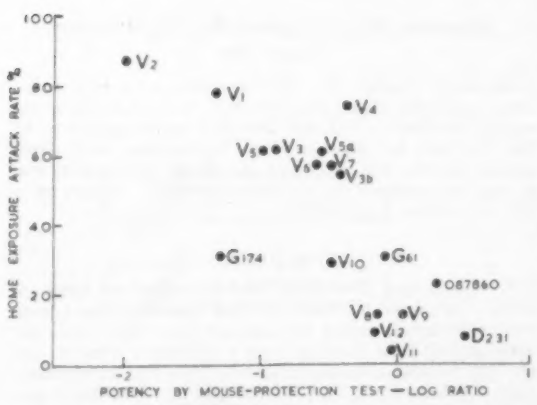

Chart showing the relationship, with 18 pertussis vaccines, between home exposure attack rate in the field and potency as estimated by the mouse-protection test.

The relationship between the home-exposure attack rates and the potency-ratios, estimated by the mouse-protection test, is shown in the Chart. There appears to be good correlation. In interpreting these results it should be remembered that both the attack rates and the potencies are subject to sampling errors which may have exaggerated or detracted from the true correlation, that attack rates are possibly subject to variations from one area or one period of time to another, and that the assumptions that the vaccines deteriorate at a constant rate of 0.2 log unit a year may be invalid. However, as the second column of Table XII shows, the different vaccines within each of the three groups were used in the field over fairly short periods of time. Consequently, a false assumption about the rate of deterioration would affect principally the relative potencies between the three groups rather than those within the groups. Even when attention is restricted to fluctuations within the three groups of vaccines, the correlation between the home-exposure attack rate and the potency-ratio is still significant. These results suggest that the mouse-protection test is of some value in predicting field results.

Field Trials and Agglutinin Tests

Table XII also shows for a number of vaccines the relationship between (*a*) the home exposure attack rate, (*b*) the agglutinin produced in mice to a dose of 10×10^8 organisms, and (*c*) the agglutinin produced in children to their course of immunization. It is evident that there is a close correlation between the production of agglutinin in mice and in children; of the 11 vaccines tested by both methods, 7 gave a poor response and 4 a decidedly higher response in both cases.

It is also evident that there is a general correlation between protection in the field and agglutinin response. Six vaccines which showed substantial protection each gave a good agglutinin response in mice, and four of these also gave a good response when tested in children. On the other hand, nine vaccines which showed poor protection each gave a poor agglutinin response in children, and seven of these also gave a poor response when tested in mice.

CONCLUSIONS

Two series of field trials were made in which 28,799 children were followed up for an average of two years after inoculation with pertussis vaccines. Severe local or general reactions were not encountered and there was insufficient evidence to show that pertussis vaccine precipitated repeated convulsions or initiated serious cerebral damage. In three cases of poliomyelitis which occurred within 28 days after injections, the site of paralysis was confined to the injected limb.

Fourteen batches of vaccine were used; their protective effect was assessed mainly on the basis of home-exposure attack rates. The nine batches of vaccine used in the first series of trials were poor, but the five batches used in the second series gave substantial protection.

As is shown in Table I, the vaccines in the first series were all made from the same strain of *H. pertussis*. They were prepared from 24- or 48-hour cultures on Bordet–Gengou medium containing horse blood or from culture in liquid medium. In all of them formalin was used as the killing agent, but some were preserved with phenol and others with thiomersalate. Between initial isolation and use in the vaccines, the strain had been repeatedly subcultured in the laboratory. The vaccines in the second series were made from a mixture of four, six, or seven freshly isolated strains which had been subcultured on very few occasions before being freeze-dried. Three vaccines were made using Bordet–Gengou medium containing sheep's blood, one using Bordet–Gengou medium containing human blood, and one using liquid medium. All were killed, and preserved with thiomersalate.

It is clear that the vaccines in the first series differed in many ways from those in the second series, but it is not

possible to say which of the differences were responsible for the widely divergent results.

The field studies showed that in the second series three vaccines (V9, V10, and V12) made in this country from strains of *H. pertussis* isolated here were as effective as the reference vaccine (V8) made with American strains and supplied by the Michigan Department of Health, and that the vaccine prepared by the State of New York Department of Health (V11) from the same American strains as the reference vaccine, but grown in liquid medium, was, in a preliminary trial, also as effective as the reference vaccine.

At the same time as the field trials were in progress, laboratory tests were made in which the vaccines were extensively tested for their ability to protect mice against intracerebral pertussis infection. Some of the vaccines were tested for their ability to produce agglutinin in mice, and sera from a number of vaccinated children were titrated for agglutinin.

There was a correlation between protection in children and three laboratory tests : (*a*) protection of mice against intracerebral infection with *H. pertussis*, (*b*) production of specific agglutinin in mice, and (*c*) production of specific agglutinin in children. Though the three laboratory tests gave results parallel with those obtained in the field, it does not necessarily follow that the laboratory tests measure directly the factor or factors responsible for the production of immunity in children. Pillemer and his colleagues (1954) have prepared from *H. pertussis* an antigenic fraction which protects mice against intracerebral infection, but which produces a very poor agglutinin response in mice (Evans and Perkins, 1955). The protective potency of this fraction in children is being tested at present in Liverpool and preliminary results suggest that it is giving protection. The mouse-agglutinin-production test therefore may not be a reliable guide to the value of all vaccines in children. Agglutinin production in children has been accepted by some workers as evidence of protective potency, and the tests reported here support this conclusion. Production of agglutinin, however, is only one of the properties of *H. pertussis* and may be different from, and not always run parallel with, protective potency. In any event it would scarcely be practicable to estimate the agglutinin response in children before each batch of vaccine produced commercially was issued for general use.

Of the three laboratory tests, therefore, the mouse intracerebral challenge test is considered, on the basis of present evidence, as the most satisfactory. It is correlated with protection in children, and in mice it measures protection from infection with a virulent strain of *H. pertussis*. A British standard pertussis vaccine has been established in terms of which the potency of other vaccines may be assayed by means of comparative tests. The standard has been prepared from vaccine V12 (Table I), which gave substantial protection in the field, by freeze-drying in 6% dextran. No instability has been detected in the dried standard, and its use in comparative tests will be the subject of a separate communication (Armitage and Perry, 1956).

In view of these results it would seem wise before the issue of a vaccine for use in children to submit it to the mouse intracerebral protection test to ensure that it has an adequate potency in relation to the British standard vaccine. It is also clear that a vaccine need not necessarily be made by the Michigan method ; the results of the present trials show that one produced from cultures made in a liquid medium can give equally good results.

SUMMARY

In two series of field trials, 14 pertussis vaccines were tested for their protective potency in 28,799 children. The vaccines used in the first series of trials were poor, but those in the second series gave substantial protection, which was maintained for at least two and half to three years after vaccination.

At the same time as the field trials were in progress, laboratory tests were made in which the vaccines were tested for their ability to protect mice against intracerebral pertussis infection. Some of the vaccines were also tested for their ability to produce specific agglutinin in mice and in children.

A comparison between the field and laboratory results showed some correlation between the potency of vaccines in protecting children and their ability to protect mice against intracerebral infection. There was also evidence of a correlation between protection in children and ability to produce agglutinin in both mice and children.

It is concluded that in future only those pertussis vaccines which have been shown, by the intracerebral mouse-protection test, to have an adequate potency in relation to the British standard pertussis vaccine should be issued for use in children.

The Whooping-cough Immunization Committee of the Medical Research Council and the medical officers of health in the areas where the trials were made are grateful to the parents who consented to have their children injected. They wish to thank Glaxo Research Laboratories, the Lister Institute of Preventive Medicine, the Michigan Department of Health, the State of New York Department of Health, and the Wellcome Research Laboratories for the free supply of the pertussis vaccines, and the World Health Organization for its interest and for some financial help towards the cost of the second series of trials. They particularly wish to record their indebtedness to Dr. Pearl Kendrick, corresponding member of the Committee, who gave help and advice on the preparation of the vaccines during visits to this country and also by correspondence. The vaccine for the preparation of the British standard pertussis vaccine was generously provided by Glaxo Laboratories.

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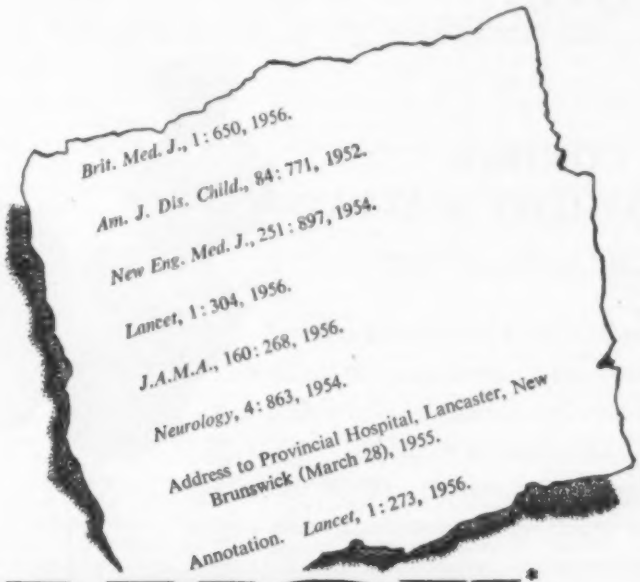
Medical Memorandum

Repeated Delayed Splenic Bleeding Into the Lesser Sac

Spontaneous rupture of a normal spleen is a rare occurrence, and only about 100 cases have been reported in the world's literature. The case described below appears to be the first recorded instance where haemorrhage took place almost entirely into the lesser sac of the peritoneum, and is the first example of spontaneous splenic rupture in a case of arterial hypertension.

CASE REPORT

A woman aged 29 was admitted to hospital on April 14, 1951. Two days previously she had been discharged from another hospital, having had an operation there about six weeks before "for bleeding from a mesenteric vessel." On the day of admission she took a laxative for constipation, after which generalized abdominal pain and vomiting began and continued up to the time she was examined (3 p.m.). On direct questioning she admitted that about 24 hours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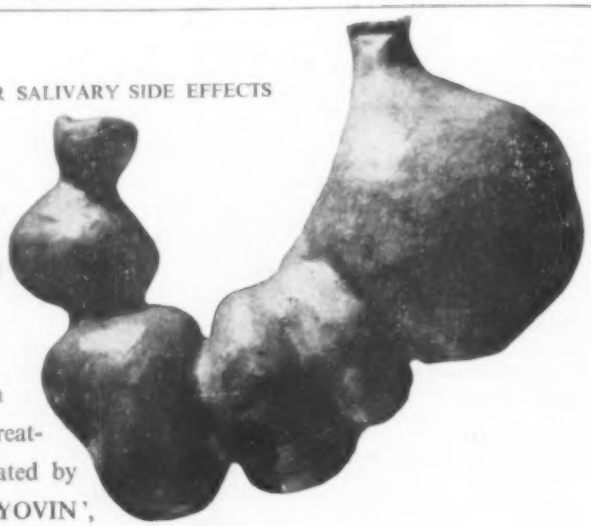

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previously she had had left shoulder-tip pain which had continued for several hours, but it had disappeared at the time of examination. She felt very weak. She said she had some "heart trouble," but that her symptoms of that complaint, chiefly headaches, had been much less noticeable during the past few weeks. Her last menstrual period was in February, 1951. No other symptoms were present. Her doctor sent her to hospital with a diagnosis of ? ruptured ectopic gestation, ? internal haemorrhage.

Two previous pregnancies were normal. She had had occasional bouts of epistaxis, heavy menstrual periods, and excessive bleeding following dental extractions. The previous hospital admission had been advised because of symptoms similar to those presenting now. In addition, whilst an in-patient there, about two weeks previously, she experienced a bout of abdominal pain and vomiting lasting a day or so, which was diagnosed as "gastritis." Her mother had died at 36 years of age from "a stroke."

The patient was a thin, pale woman, anaemic and shocked. The pulse rate was 130 a minute, temperature 97° F. (36.1° C.), respiratory rate 20, blood pressure 90/? mm. Hg. Examination revealed no gross cardiac enlargement; an apical systolic murmur was present. The lungs were normal. In the abdomen, distension was obvious. A healed scar extended from the pubis to half-way between the xiphoid and umbilicus. There was no rigidity, but generalized tenderness was found. Peristalsis was absent. Vaginal examination revealed no abnormality. Later, under general anaesthesia, a mass was palpable in the epigastrium. It was dull, and the dullness was continuous with liver dullness. A provisional diagnosis of intraperitoneal haemorrhage ? due to leaking splenic aneurysm was made.

After resuscitation, operation was undertaken on April 15. Through a midline epigastric incision the mass previously felt was seen to be the stomach pushed forward by a lesser sac full of old blood clot. There was unclotted blood in the greater sac. The spleen was adherent to the diaphragm and not easily mobilized, and it was removed; the splenic vessels had previously been ligated in continuity proximally, lest the site of section be placed distal to a ruptured aneurysm of the splenic artery. The abdomen was closed in layers and a stab drain inserted.

With the spleen were two splenculi and the tail of the pancreas. The weight of the total specimen was 450 g. Most of the upper half of the organ was occupied by old blood clot, which had disorganized the pulp. There was a tear in the capsule on the diaphragmatic surface of the spleen, but no large subcapsular haematoma otherwise. The haematoma surrounded the pedicle. No aneurysm was found. The splenic vein was thrombosed.

Convalescence was protracted owing to the development of a *Staphylococcus aureus* coagulase-positive bacteriaemia, which was finally controlled with chlortetracycline. On discharge her blood pressure was 195/140 mm. Hg.

On August 11 she was readmitted because of intractable vomiting. She stated that polyuria and polydypsia had appeared since the operation. She died on September 17.

Post-mortem examination (Dr. E. Milford Ward): Tuberculous meningitis, without evidence of tuberculosis elsewhere, was found. Heart: marked hypertrophy of the left ventricle. Both kidneys were reduced in size. The capsules stripped with difficulty and the surfaces were coarsely scarred. Histologically they showed the picture of chronic non-suppurative pyelonephritis.

COMMENT

This was an interesting clinical problem of diagnosis. Common causes of severe anaemia (Hb 29%) in a female are nutritional, or due to bleeding from the genito-urinary or gastro-intestinal tracts. Other possibilities considered here were splenic infarction from subacute bacterial endocarditis, and polyarteritis nodosa acuta. But no other signs of endocarditis were present, and muscle biopsy done at laparotomy was negative.

The presence of essential hypertension favoured the possibility of an arterial source of bleeding, such as a leaking aneurysm. Chevallier and Bernard (1944) have shown that vascular arterial lesions are the second commonest cause of haemoperitoneum in women, although occurring 25% less often than in men. It is rare to make a correct preoperative diagnosis. Of 41 cases previously reported, only 2 were accurately diagnosed.

The occurrence of this case completes the possible anatomico-pathological picture of haemorrhage from the spleen. Recalling the fact that this organ lies in relation to two peritoneal lined cavities, and that a postero-lateral relationship to the kidney brings it into contact with an extraperitoneal area, there are three possible ways in which symptoms and signs may present: (1) the commonest is bleeding into the greater sac, diagnosis often being confused with other causes of peritoneal irritation; (2) the next most frequent one is rupture into the lesser and greater sacs, a pancreatic lesion being most often diagnosed; and (3) the rarest is extraperitoneal extension into the loin, where a renal lesion is usually suspected. The present case is the first in which major and repeated bleeding took place into the lesser sac.

In several cases of normal spleens undergoing rupture a predisposing cause has been found. Undue mobility due to absence of the phrenico-colic ligament is said to occur in 2% of subjects (Susman, 1927). A vascular abnormality confined to the spleen—namely, angioma—has been once reported (Mondor and Boutron, 1938), but such a spleen is not truly "normal." Various alterations in contour with partial deficiency have also been found, but rupture did not always take place at the site of abnormality. It was impossible to discover a predisposing cause in this case.

The commonest event initiating spontaneous rupture is sudden increase in blood volume in the splenic vein. In the absence of any pertinent history this could not be established here. According to Price (1950) aseptic infarction of the spleen is commoner than realized and is often found in cardiac disease. In the absence of other evidence it must be assumed that this was the primary event in the present subject: an infarct was certainly shown microscopically.

Splenic histology is notoriously difficult to interpret. Wohl (1925) noted that, by the age of 36, 50% of spleens showed evidence of intimal thickening and hyaline change in the Malpighian bodies. Evidence of hypertensive disease is difficult to find unequivocally in this organ and was not found here, although other arteries in the body showed a characteristic histological picture of arterial hypertension.

It could not be established what the initial event producing haemorrhage was, and the relation of coexisting arterial hypertension remains speculative if not entirely coincidental.

I wish to thank Mr. J. C. Barrett for permission to publish this case and also Dr. E. Milford Ward, who reported on the specimens and performed the necropsy.

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To help local authorities in their Clean Food campaigns the Ministry of Health has produced a new coloured poster on the theme "Hands Spread Germs." A series of pictures and slogans emphasizes the importance of covering cuts and sores, fingering food as little as possible, and washing hands thoroughly before preparing food.

Reviews

BIOCHEMISTRY AND PHYSIOLOGY OF BONE

The Biochemistry and Physiology of Bone. Edited by Geoffrey H. Bourne. (Pp. 875; illustrated. £7 3s.) London: Academic Books Ltd. 1956.

This book comes out at a most suitable moment, since there is now an increasing interest in the subjects of bone diseases and of disorders of calcium metabolism. It consists of a series of articles by well-known authorities, who review in turn a wide range of subjects, starting with anatomical and structural matters and proceeding to the microscopy and ultrastructure of bone. It continues with further considerations of the growth of bone and of the effects of various vitamins and hormones. The articles naturally differ from each other in style and content, some comprising uncritical compendia of the work on the subject with full references, others being more critical and selective and therefore more readable. A good example of the latter is the chapter by F. C. McLean on the parathyroid glands and bone, which should do much to remove the many current misconceptions on this matter. The book does not deal, except in the most cursory manner, with many of the interesting current medical problems of bone disease and its treatment, but nevertheless it should be a useful work of reference for those whose specialty necessarily overlaps other specialties, in particular orthopaedic surgeons, paediatricians, and urogenital surgeons.

C. E. DENT.

COMPLICATIONS OF REGIONAL ANALGESIA

Complications of Regional Anesthesia: Etiology, Signs and Symptoms, Treatment. By Daniel C. Moore, M.D. (Pp. 291 +xv; illustrated. 75s.) Oxford: Blackwell Scientific Publications. 1956.

Regional analgesia for surgery is by and large a rarity in this country. A combination of a critical public, antipathetic surgical opinion, and a high standard of general anaesthesia have contributed to this state of affairs. On the other hand, nerve-blocks for a variety of therapeutic and diagnostic reasons are on the increase. A knowledge of the complications which may follow these procedures is therefore important, and a comprehensive review of these is now available. Drawing from his own large experience and from the literature, Dr. Moore includes not only the local and general complications of nerve-blocks, but also those of spinal and epidural analgesia. In a separate section entitled "Incidental Complications" he gives excellent brief accounts of such complications as atelectasis, amnesia, and retention of urine. This book, with its high standard of writing and illustration, is easily one of the best and most important in its field, the long list of references at the end of each chapter being particularly valuable. In case a comprehensive and scholarly book of this sort may give the wrong impression, the author himself writes as follows in his introduction: "Although this book is entirely devoted to the complications of regional block procedures, this should not be construed to mean that complications following regional nerve blocking occur frequently, or that this type of anesthesia is more dangerous than other types." This book is one of outstanding merit and will repay careful study.

W. W. MUSHIN.

STRESS

Fifth Annual Report on Stress, 1955–56. Edited by Hans Selye, M.D., Ph.D., D.Sc., F.R.S.(Canada), F.I.C.S., and Gunnar Heuser, M.D. (Pp. 815; illustrated. $20.) New York: MD Publications Inc. 1956.

This *Annual Report on Stress* has the same editors and the same general format as its predecessor. The first 100 pages give the views of Selye on the general physiology and pathology of stress with emphasis on the stress concept as he sees it in 1955, and a review of the principal lines of research in this field during the same year. The next 100 pages contain an excellent series of review articles by various workers: "Primary Aldosteronism, a New Clinical Entity," by J. W. Conn and L. H. Louis; "Hormonal Influences on Inflammation and Detoxification," by T. F. Dougherty and R. D. Higginbotham; "Stress and Catechol Hormones," by U. S. von Euler; "Adrenal Influences upon the Stomach and the Gastric Response to Stress," by S. J. Gray, C. G. Ramsey, R. Villarreal, and L. J. Krakauer; "Some Questions Relating to the Role of the Adrenal Cortex in the Etiology of Disease," by D. J. Ingle; "Adrenocortical Secretion and Factors Affecting that Secretion," by D. H. Nelson; "Neurosecretion," by E. Scharrer; "Some Observations on Psychiatric Stress in Infancy," by R. A. Spitz; and "Cortisone in Relation to Lymphoid Tissue and Immunity," by H. C. Stoerk. The special physiology and pathology of stress occupy the next 340 pages and take the form, now usual in these volumes, of a series of annotations of the results described in the many publications covered. I had some difficulty at first in finding the way through this section, but the table of contents and the index were of use in this respect. The alphabetical list of between 5,000 and 6,000 references, complete with titles, forms one of the most valuable sections. A reference copy of this book should certainly be available in every medical library.

G. W. HARRIS.

SKIN TUMOURS

Tumors of the Skin. By Herbert Conway, B.S., M.S., M.B., M.D., F.A.C.S. (Pp. 267+xiv; illustrated. 97s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956.

The first half of this book is devoted to benign tumours and is well presented, though it is not as complete as one would expect in a work devoted solely to the subject of skin tumours. The text opens, for instance, with sebaceous cysts, but no mention is made of their naevoid and familial features or of the association with intestinal polyposis and cancer. The only treatment mentioned is surgical excision. Angiomata are adequately reviewed, though the author does not seem convinced that true cavernous angiomata can recover spontaneously. In relation to malignant lesions, which take up the latter half of the book, the field is again not covered in detail, as might be expected, and much space is given to illustration of surgical procedures. A good deal more text might usefully have been devoted to fuller clinical descriptions of the ordinary basal and squamous-celled carcinomata and to the causative and predisposing factors. Very much more might have been said of the intra-epidermal and superficial carcinomata. The erythroplasia of Queyrat is mentioned, but not the plasma-celled balanitis which exactly mimics this type of carcinoma but is purely inflammatory. There is no mention of the erysipelatoid and telangiectatic carcinomata of skin seen particularly in relation to breast cancer, nor is there adequate discussion of the mode of spread in the skin. It is now well recognized that a lesion described under the terms "molluscum sebaceum," "kerato-acanthoma," or "pseudo-epithelioma" has until the last few years been diagnosed by clinicians and pathologists alike as an acute epithelioma, whereas the condition is benign and clears spontaneously. This disease is not mentioned. The impression is given that all malignant melanomata are gravely malignant. The lentigo maligna, the relatively benign type seen particularly in the elderly, is not discussed.

The approach to the problem of skin tumours is very much that of the surgeon, and especially the plastic surgeon. For the student there is not much more than he will get in the ordinary textbook, and the work is not adequate for the specialist. Nevertheless it is of value to have a consideration of neoplasms in this fashion, and the book will, as the author intends, serve as a ready reference text and as an aid to diagnosis. It is well produced and the numerous illustrations are good.

J. T. INGRAM.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY AUGUST 25 1956

HYPOGLYCAEMIC SULPHONAMIDES

Ten months ago two groups of German physicians[1 2] announced that many diabetics could dispense with insulin injections and have their diabetes treated by tablets. The drug used was a sulphonamide, sulphanilyl-*n*-butylurea (BZ 55, "carbutamide," "invenol," "nadisan"). As Professor F. G. Young points out in the opening article in this week's *Journal*, the discovery that some sulphonamides had a hypoglycaemic action was by no means new, for it was originally reported by M. Janbon and his colleagues[3] in Montpellier in 1942, and French workers[4] have been studying the biochemical mechanisms involved since that time. It was in Germany, however, that these drugs were first used on a large scale for the treatment of diabetes. The original reports made it clear that BZ 55 had no place in the treatment of the young insulin-deficient diabetic, but it was claimed that many of the older more stable diabetics could use it instead of insulin injections. Even with this limitation the reports aroused great interest both among diabetic patients and among their doctors. The Hamburg results were brought up to date by a further article from F. Bertram and his colleagues[5] early this year, and reports from other countries in Europe[6–11] and elsewhere[12–15] have confirmed the German claims.

In Britain and in the United States there was considerable scepticism. From observation of the German clinics it was clear that too many of their diabetics were treated with insulin, and that dietary control was largely ignored even in the grossly obese; and it was felt that although in Germany these patients might be treated with insulin and could be switched satisfactorily to BZ 55, in a British clinic many would be dieted without insulin and that BZ 55, even if the German claims were sustained, would be indicated only in comparatively few cases. Another reason for scepticism was the uncertainty over the way in which the drugs produced their effect on the blood sugar, and the possibility that long-continued use would lead to undesirable metabolic or enzymatic disturbances. Finally, the record of the sulphonamides as a cause of fatal toxic reactions, blood dyscrasias, and allergic responses is a bad one, and it seemed unlikely that any member of this group of drugs could be given safely for a period of years. Dangerous side-effects may have to be accepted if the drug in question is the only one that can be used for a seriously ill patient; with mild diabetics, however, there is already a safe physiological remedy available, and any proposed alternative must be equally innocuous.

We publish this week six articles reporting the observations of British workers who have been treating patients with this drug. The reports from Edinburgh (p. 433) and the Whittington Hospital in London (p. 440) are accounts of extensive in-patient trials. Out-patient experience or less comprehensive in-patient studies are reported from King's College Hospital (p. 445) and the Middlesex Hospital in London (p. 451) and from Dundee (p. 448) and Glasgow (p. 452). A total of 193 patients are reviewed; of these about 170 fulfilled the German criteria as being likely to respond to BZ 55 and 125 did so (73%). These studies confirm that the type of patient responsive to this treatment is the middle-aged or elderly diabetic who has never had ketosis and who needs less than thirty units per day of insulin (a few patients on larger doses did respond satisfactorily). The report from the Whittington Hospital suggests that if the fasting blood sugar after stopping insulin is over 275 mg. per 100 ml. satisfactory response is unlikely. In general, grossly obese subjects were excluded from the British trials. One point that the reports bring out is the danger of stopping insulin in what seems to be a suitable stable diabetic not apparently liable to ketosis. Several clinics encountered patients of this type who developed severe diabetic ketosis within a few days, and it is clear that if transfer of an insulin-taking diabetic to sulphonamide therapy is contemplated the patient must either be seen daily after stopping the insulin or admitted to hospital.

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[14] Leibel, B. S., *Canad. med. Ass. J.*, 1956, **74**, 979.
[15] Ridolfo, A. S., and Kirtley, W. R., *J. Amer. med. Ass.*, 1956, **160**, 1285.
[16] Kinsell, L. W., *et al.*, *Science*, 1956, **123**, 585.
[17] More, R. H., McMillan, G. C., and Duff, G. L., *Amer. J. Path.*, 1946, **22**, 703.
[18] *Dtsch. med. Wschr.*, 1956, **81**, 823 and 887.
[19] Ibid., 1956, **81**, 826.
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[21] Miller, M., and Craig, J. W., *Metabolism*, 1956, **5**, 162.
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[26] Achelis, J., and Hardebeck, K., ibid., 1955, **80**, 1452.
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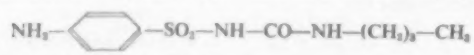
[28] Loubatières, A., de Laclos, C. F., and Bouyard, P., *Sem. Hôp. Paris*, 1956, **32**, 2358.
[29] Ashworth, M. A., and Haist, R. E., *Canad. med. Ass. J.*, 1956, **74**, 975.
[30] Mirsky, I. A., Perisutti, G., and Diengott, D., *Metabolism*, 1956, **5**, 136.
[31] Hawkins, R. D., Ashworth, M. A., and Haist, R. E., *Canad. med. Ass. J.*, 1956, **74**, 972.
[32] Clarke, D. W., *et al.*, ibid., 1956, **74**, 966.
[33] Mohnike, G., and Knitsch, W., *Dtsch. med. Wschr.*, 1956, **81**, 891.
[34] Vaughan, M., *Science*, 1956, **123**, 885.

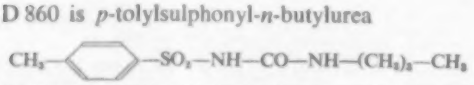
Attempts were made to select suitable cases by a test in which the blood sugar is followed for five or six hours after a large oral dose of the drug. The results were disappointing, but it does seem that good selection can be made purely on clinical grounds, one group of workers having 23 successes out of 24 patients.

The most disturbing feature of the British reports is the description of the side-effects observed. Both in this country and abroad sulphonamide rashes have been encountered: the incidence in this British series of cases is about 9%, but the rash invariably cleared when the drug was stopped. Much more serious are the alterations in the blood picture. The original German reports[1,2] stated specifically that there were no changes in the blood count. From the United States there has been a report[15] of severe leucopenia (1,900 W.B.C. per c.mm.) and from the Middlesex Hospital in this country (p. 451) of neutropenia (2,100 W.B.C. per c.mm.; 10% polymorphs). The Edinburgh workers mention persistent leucopenia, and L. W. Kinsell and his colleagues[16] have seen leucopenia with bigger doses. One patient who developed severe leucopenia was kept on the drug and the blood count returned to normal[12]—a procedure that few would recommend. In Edinburgh thrombocytopenia was found in eight patients and purpura occurred in two. Fatal reactions believed to be due to BZ 55 have occurred in the United States—in one case agranulocytosis was the cause and in another sulphonamide allergy of the type described by R. H. More and his colleagues[17] ten years ago. It is not yet known where the BZ 55 used in these cases was manufactured. The possibility of some impurity cannot be excluded, although it seems unlikely, and we wish particularly to draw attention to "A Warning Note" published at p. 454 in this issue. It is the considered opinion of the signatories of this note that BZ 55 should at present be used only under careful hospital supervision, and some would even go further and recommend the discontinuance of trials until more is known about the toxicity of the drug.

The possible danger attached to the use of BZ 55 has increased the importance of another hypoglycaemic compound recently described (D 860, "rastinon," "orinase").[18] BZ 55 has the formula



D 860 is *p*-tolylsulphonyl-*n*-butylurea



It differs from BZ 55 in having a methyl group instead of an amino group on the benzene ring and might therefore have less tendency to produce blood dyscrasias; this substitution also leads to loss of all antibacterial action. Clinical reports[19-23] show that it is as effective as BZ 55, with perhaps less tendency to produce skin reactions, and as yet there are no reports of any blood dyscrasias. Because of the loss of the amino group the concentration of the drug in the blood cannot be estimated by the procedure devised by Bratton and Marshall, although a method by which it can be done has been worked out.[24] It is excreted in the urine as an oxidation product which may give a false positive reaction in the sulphosalicylic acid test for proteinuria.[25] The drug is now undergoing trial at a number of centres in this country, but after the experience with BZ 55 it will be some time before any recommendations can be made.

The mode of action of the hypoglycaemic sulphonamides remains obscure despite a year's intensive research in many countries. German workers have suggested that these compounds damaged the α-cells of the pancreatic islets and stopped the production of the hormone glucagon, which raises the blood sugar.[26] The changes in the α-cells, however, are inconsistent, and other possibilities have to be considered. C. H. Best[27] has recently reviewed the position. Indirect action through another endocrine gland has been excluded. It seems clear that some insulin must be present for the compounds to have a hypoglycaemic action. The possibility that they increase insulin production, originally suggested by A. Loubatières,[28] has been further studied by R. E. Haist[29] in Toronto, who gave very large doses of BZ 55 to rats and noted islet hypertrophy. A second theory of their mode of action is that they interfere with insulin destruction, and I. A. Mirsky[30] has reported that both BZ 55 and D 860 reduce insulinase activity of the rat liver. The third possibility is that they potentiate insulin by action on enzymes, probably in the liver.[31] It has been established that the release of glucose from liver slices is reduced by these compounds,[32-34] but information about how this is achieved is not yet available.

There can be no doubt that the hypoglycaemic sulphonamides will lower the blood sugar in many mild, stable, middle-aged diabetics. Some of these patients who need insulin to keep their blood sugar at a reasonable level may be able to dispense with injections and take tablets instead. But the action of these compounds differs from that of insulin,[24] and although they may lower the blood sugar they need not necessarily correct the other metabolic disturbances of diabetes. The British and American experience suggests that BZ 55 is a dangerous substance unsuitable for long-term control of mild diabetics. D 860 may prove safer, but prolonged trial will be needed. Three questions have to be answered about this compound and other similar ones that may be produced. First, do they ever produce dangerous

side-effects? Secondly, what exactly is their mode of action? If it is by enzyme inhibition, can this be harmful if continued for years? Thirdly, although the blood sugar may be lowered by these compounds, do they correct the other metabolic consequences of diabetes? Will they prevent the development of retinitis and nephropathy? It will take a long time to obtain satisfactory answers to these questions, and until they are answered the hypoglycaemic sulphonamides must be regarded as experimental and used only under strictest supervision.

IMMUNIZATION AGAINST WHOOPING-COUGH

Five years ago we published the report[1] of the Medical Research Council's Whooping-Cough Immunization Committee on a series of controlled trials of pertussis vaccine. In these trials batches of vaccine from three manufacturers, two American and one British, were put to the final test of efficacy: the incidence of whooping-cough was measured by careful observation over a period of 24 months or more in a group of children 6 to 18 months old and compared with that in a similar group injected only with an anticatarrhal vaccine. The parents of all the children had agreed to their inclusion in the trial and the children were allocated randomly to the groups receiving pertussis or anticatarrhal vaccines, so that neither parents nor the medical staff observing the children knew which vaccine any individual child had received. All the batches of vaccine thus tested provided substantial protection, the attack rates being less and the disease when it occurred milder in the vaccinated than in the control children. Commenting on this report at the time, we wrote: "What is particularly needed now is some laboratory yardstick which will differentiate between good and poor vaccines," and in fact it has been the lack of a satisfactory test to measure the antigenic potency of pertussis vaccines that has delayed official approval of combined diphtheria-pertussis prophylactics. Before the controlled trials were completed further field trials in conjunction with laboratory tests had already been started in an attempt to provide this yardstick, and the report on these combined investigations appears elsewhere in this issue (p. 454). Because of the success of vaccine in the controlled trials it was no longer possible to have a control group given a placebo, and instead two or more vaccines were compared in parallel in each subsequent trial. In each of the series of seven trials carried out during the years 1948 to 1951 volunteer children were allocated in rotation to groups receiving three British vaccines: in total nine batches of vaccine prepared from the same strain of *H. pertussis* by several different methods were used, and just under 10,000 children kept under observation. In the 1951–4 series of eleven trials five vaccines were used, each prepared from several strains of *H. pertussis*. A large batch from the Michigan Department of Health, whose vaccine gave greatest protection in the original controlled trials, was used in about half the children in each trial. The other half were given one of three British vaccines prepared by the Michigan method or one made by the State of New York Department of Health from liquid-medium culture of the same strains used in the Michigan vaccine. The 19,000 children observed in these later trials were allocated to the group receiving the Michigan reference vaccine or to the group receiving the other vaccines according to whether their birthdays fell on odd or even days of the month. In other respects the conduct of the trials in both series followed the pattern of the earlier controlled trials, and the performance of the vaccines was assessed by measuring the incidence of pertussis in three ways—the attack rate per 1,000 "child-months" of observation, the percentage attack rate in children exposed to infection in their own homes, and the percentage attack rate in children exposed elsewhere.

No large differences were observed between the protection afforded by the vaccines used in the 1948–51 series of trials or between those used in the 1951–4 series. However, all three measures of incidence were substantially lower in the latter trials. For example, the attack rate in the 1948–51 series among children exposed to the disease in their homes was 69% overall, and in only one small trial was less than 50%. In 1951–4 this was 14% overall, with a maximum of 29% in one trial. In all the previous controlled trials combined, the corresponding rate was 87% for unvaccinated and 18% for vaccinated children, suggesting that unless the infectivity of pertussis or the general level of immunity had changed considerably the 1948–51 series of vaccines were poor, whereas all the 1951–4 series were probably giving good protection. Although there was no control group to substantiate this interpretation it was neatly confirmed in the 1951–4 studies. In three of the larger participating areas records were kept of the incidence of pertussis in households in which vaccinated children and their unvaccinated siblings were exposed to infection by a primary case in the family. In 56 such households there were 69 vaccinated and

[1] The Prevention of Whooping-Cough by Vaccination—A Medical Research Council Investigation, *British Medical Journal*, 1951, 1, 1463.
[2] *Lancet*, 1954, 1, 1257.

62 unvaccinated children exposed to risk. Only fourteen (20%) of the vaccinated developed pertussis compared with 51 (82%) of the unvaccinated.

The laboratory investigations conducted in parallel with these field trials were of three kinds—the mouse-protection test, the measurement of the ability of the vaccines to produce agglutinin in mice (the mouse-agglutination-production test), and the measurement of the ability of the vaccines to produce agglutinin in children. In the first of these tests mice were injected intraperitoneally with graded doses of vaccine, and the level of protection measured by injecting 14 days later a challenge dose of virulent *H. pertussis* intracerebrally. An alternative test by which the challenge dose of bacteria was given intranasally was found to be less sensitive and was abandoned. From the proportion of deaths observed within 14 days of challenge, the dose of vaccine required to protect 50% of animals (ImD_{50}) was calculated. In each test two vaccines were compared simultaneously, one of which was a reference vaccine. The error of this test was found to be large despite careful standardization of reagents, procedures, and the use of mice of inbred stock. In all, 18 vaccines, including some used in the controlled field trials, were tested by this method. The tests were carried out over a period of years, and from repeated tests on the same vaccines the ImD_{50} values suggested a deterioration of about 40% in potency per annum, and this assumption was made when the final order of potency for the vaccines was calculated from the results of this test. The mouse-agglutination-production test was introduced late in the field studies and could not be applied to all the vaccines. Groups of mice were given two injections at a 14-day interval and the agglutinin titre determined 10 days after the second dose. The vaccines were graded according to the agglutinin response to a fixed dose of organisms. Two independent studies were made of the ability of some of the vaccines used in the field to produce specific agglutinin in children. The technical details differed in some particulars, but the results obtained on the same vaccines were similar and the two series were combined in grading the vaccines thus tested.

The results of these three laboratory tests were related to the attack rate among vaccinated children exposed to the disease in their own homes—the most stable measure of performance of a vaccine in the field. The report states that though field and mouse-protection tests occasionally put vaccines in different orders of potency there were no definite contradictions, and the general correlation, though not high, suggested that the mouse-protection test was of some value in predicting the efficacy of a vaccine in protecting children against pertussis. There was a close correlation between the production of agglutinin in mice and in children, and a definite but less close correlation between the results of these tests and prophylactic potency of the vaccines judged by the field trials.

Although there is correlation between the protection of children in the field and the results of the three laboratory tests, it does not follow that the laboratory tests measure directly the factor responsible for producing immunity in children, and this must influence the choice of test for standardization of commercial vaccines. As a yardstick the production of agglutinin in mice might be favoured had not L. Pillemer and his colleagues[3] at Western Reserve University prepared from *H. pertussis* an antigenic fraction which protected mice against intracerebral infection but gave a very poor agglutinin response. This antigen is now undergoing test in a field trial in this country. It would plainly be impracticable to estimate the agglutinin response in children before each batch of vaccine produced commercially was issued for general use, and the M.R.C. report therefore recommends that in future only those vaccines which have been shown by the intracerebral mouse-protection test to have an adequate potency should be released. In order to establish a British standard pertussis vaccine for use in such comparative tests, one of the British vaccines which gave substantial protection in the field in the 1951–4 trials has been freeze-dried, and this dried product, unlike the parent liquid vaccine, has shown no instability. Since vaccines made by both Michigan methods and from cultures made in a liquid medium gave equally good results, the report makes no specific recommendations about the appropriate method of manufacture.

AN EXTERNAL DEFIBRILLATOR

A defibrillator—an apparatus for applying an electric current directly to the exposed heart—is now generally accepted as a necessary piece of emergency equipment during cardiac operations, and defibrillation with this instrument combined with cardiac massage has now proved a safe and effective method of treatment. The use of the defibrillator presupposes that the patient is in the operating theatre with the heart exposed or that immediate facilities are available for doing this. Apart from surgical or anaesthetic emergencies, however, ventricular fibrillation may be a cause of sudden death in cardiac infarction, Stokes–Adams disease, and toxic reactions to digitalis, quinidine, or procaine amide. In these conditions facilities for opening the chest, applying the defibrillator, and performing cardiac massage are seldom

[3] Beck, C. S., Weckesser, E. C., and Barry, F. M., *J. Amer. med. Ass.*, 1956, **161**, 434.
[4] Zoll, P. M., *et al.*, *New Engl. J. Med.*, 1956, **254**, 727.

medical relief services, which remove the chief initial itself is a common disease. On the other hand, two-

available, though C. S. Beck and his colleagues[3] at Cleveland have recently described the revival by these means of a physician who "died" from a heart attack outside a hospital and was having cardiac massage in an operating theatre within five minutes: the ventricles were found to be in coarse fibrillation, and after several unsuccessful shocks defibrillation was at last achieved half an hour after the onset of the attack. The patient made a good recovery.

P. M. Zoll and his colleagues[4] at Boston have now described the termination of ventricular fibrillation in man by externally applied electric shock. The external defibrillator is built on the same principle as a direct defibrillator, but the strength of the countershock applied is much greater, the voltage used being in the region of 200 to 700 volts instead of 120 to 150 volts in the case of the direct defibrillator. Large copper electrodes, mounted on heavily insulated handles and smeared with electrode paste, are held firmly in place against the chest wall, one to the left of the sternum and the other on the anterior axillary line. The duration of the current applied is fixed at 0.15 second. Defibrillation was successfully achieved with this instrument in four patients. The episodes of ventricular fibrillation occurred in the course of myocardial infarction, after intravenous procaine amide for rapid arrhythmia, in digitalis intoxication, and in Stokes–Adams disease. Although defibrillation was achieved eleven times in these patients, only the patient with Stokes–Adams disease recovered, and he was also the only patient in whom resuscitation was accomplished within two to four minutes of the onset of fibrillation, the interval in the remaining patients being not less than seven minutes.

The external defibrillator represents a real advance in methods of resuscitation, but in spite of its theoretical advantages in the avoidance of a thoracotomy its usefulness will probably prove to be restricted. For successful resuscitation it must probably be applied within less than five minutes of the onset of fibrillation, which presupposes that the instrument is already set up by the patient's bedside and that an electrocardiogram is also immediately available—conditions which are very unlikely to be fulfilled unless the episode of ventricular fibrillation has been anticipated.

OPIUM IN INDIA

Attempts to suppress the abuse of opium and its derivatives and to limit the supply to their indispensable administration for the relief of pain have been made by various International Conventions, from the first in 1912 until the most recent Opium Protocol of the United Nations in 1953. A comprehensive survey of the opium position, both past and present, in India has been made by Sir Ram Nath Chopra,[1] focusing attention on its quasi-medical use as distinct from addiction or legitimate therapy. As early as 1813 the Government of India attempted to restrict the habit of opium eating, but in 1895 a Royal Commission concluded that the consumption of opium by adults and its administration to children were based on an age-long tradition of belief in its efficacy as a common domestic remedy, and that this generally moderate use had not resulted in any extensive physical or moral degradation. This view was upheld in 1911 by the representative of the British Government, Lord Harding, who stated that it would not be practicable to draw a distinction between the medical and non-medical uses in the distribution and sale of the drug and that it was not necessary to prohibit the manufacture and sale of opium except for medical purposes in British India. In spite of the criticism, both local and international, evoked by this policy it was not until 1946 that the Government of India decided at first to prohibit the smoking of opium and later to discourage its production except for medical and scientific use.

Opium has been extensively used by Hindu and Mohammedan physicians since the fifteenth century, both internally and externally as a "paint" application, for the alleviation of pain such as headache and toothache, and for its astringent qualities in diarrhoea and dysentery. In 1928 an investigation by Chopra and his co-workers into the problem of opium consumption in India showed, surprisingly, that only a small fraction of the population indulged in opium so habitually as to become addicts, and that when addiction did follow it was usually initiated by its use for some disease or ailment. The drugging of infants as a cure for abdominal discomfort, diarrhoea, and teething troubles, and also to keep them quiet while the mother was at work, was undoubtedly very prevalent in certain parts of India up to about 1934. The dosage, said to be equal in weight to a poppy seed—$\frac{1}{16}$–$\frac{1}{4}$ gr. (12–24 mg.)—was generally begun at the age of three weeks to three months, and increased gradually to obtain the desired effect. Most of these children were small, emaciated, and anaemic, with protuberant abdomens, conjunctivitis, corneal ulcers, and purulent otitis media. With adults, the quasi-medical consumption of various preparations and infusions made from the unlanced capsules of the poppy heads has long been a favourite method of indulgence in the drug, particularly the beverage known as "post." The average daily amount of 5 to 10 capsules, soaked in water, strained, diluted, and mixed with sugar, gives a dose of 3–5 gr. (0.2–0.32 g.) of alkaloids, comprising a very small quantity of morphine and large quantities of narcotine, papaverine, and codeine, which appear to act more as stimulants than depressants and are probably responsible for the euphoric effect of this beverage. About 40% of habitués to "post" begin to take it in the hope of curing some ailment or illness, but when addiction is established, even with small doses, mental and physical deterioration follows, with symptoms of chronic poisoning of the nervous system, varying from excitation to eventual complete paralytic breakdown.

The smoking of opium has never presented such a serious problem of addiction in India as in China, and, except for the relatively small number of registered smokers (2,519 in 1954), is now subject to severe restrictions. Quasi-medical consumption has diminished during the last decade, owing partly to the extension of

[1] *Bull. Narcot.*, 1955, 7.

medical relief services, which remove the chief initial cause of the habit and its progress to addiction, but chiefly to the measures taken following the All India Opium Conference of 1949, particularly the recommendation which relates to "effective steps to bring down the per capita consumption to a level not exceeding the League of Nations limit" (12 lb. (5.4 kg.) for every 10,000 of population). These measures have resulted already in a decrease in consumption of about 45%. With strict control of the cultivation of the poppy, enforcement of the Dangerous Drugs Act, and legislation controlling the sale of opium, the quasi-medical use of such preparations as "post" is expected to cease entirely in the near future, and the problem of the consumption of opium in India as it existed before 1948 will no longer exist.

SJÖGREN'S SYNDROME

From 1888, when W. B. Hadden[1] first described the symptoms of what is now known as Sjögren's syndrome, to the review of it in 1956 by M. Thompson and S. Eadie,[2] the relationship of the ocular abnormality to the arthritic lesions of rheumatoid disease has remained obscure. The early observations of H. Gougerot,[3] A. W. M. Houwer,[4] and H. Sjögren[5] were made primarily from the ophthalmologist's point of view, and the widespread nature of the lesions was not generally appreciated. Now that the diagnosis is made more often it is generally agreed that kerato-conjunctivitis sicca is the essential clinical feature of Sjögren's syndrome, but well-established cases exhibit dryness of the mouth, parotid swellings, rhinitis sicca, and in two-thirds of the cases a rheumatoid type of arthritis. This variable clinical picture has been further confused by the inclusion of such disorders as Raynaud's phenomenon, skin changes of various kinds, both hyper- and hypoglycaemia, epilepsy and mental changes, achlorhydria and indigestion, to mention but a few. Some of these associations are undoubtedly coincidental, and recently the limits of the syndrome have become more clearly defined.

Of the 18 cases investigated by Thompson and Eadie, 14 (77%) suffered from rheumatoid arthritis, an equal number complained of dryness of the mouth, and 66% showed signs of laryngo-pharyngo-rhinitis sicca. These authors examined 210 patients with rheumatoid arthritis and found the incidence of kerato-conjunctivitis sicca to be 14.3%—a figure which agrees well with that of 13.4% given by S. Holm[6] and 11% by T. Stenstam.[7] Indeed, Holm found that kerato-conjunctivitis was a more common complication of rheumatoid arthritis than iritis, the incidence of which was only 1.2%. The question remains whether an association of this order of frequency indicates a pathogenetic connexion between the ocular and arthritic lesions. J. W. Henderson[8] and P. Ellman and his colleagues[9] are not entirely convinced that arthritis is an integral part of the syndrome. They point out that clear-cut evidence of Sjögren's syndrome is rare in women with rheumatoid arthritis, which itself is a common disease. On the other hand, two-thirds of patients with kerato-conjunctivitis sicca have frank arthritis or fleeting arthralgia, and many observers are prepared to consider both groups of symptoms as manifestations of a common rheumatic process.[6 10 11] Further evidence that this is so is now being brought to light. K. J. Gurling[12] has reported the association of Felty's and Sjögren's syndromes and uncovered in the literature several examples in which the features of both syndromes were present. Thompson and Eadie have also encountered the same combination, and it is of interest that D. H. Collins[13] reported that the symptoms and signs of Still's disease—another rheumatic disorder in the group of collagen diseases—could develop into those of Felty's syndrome, which is characterized by chronic arthritis, splenomegaly, and leucopenia. Disease of the joints is a feature in all three disorders.

The lack of opportunities for examining post-mortem material has hindered the understanding of the basic pathological changes, most studies being based on biopsy specimens from the conjunctiva and the lacrimal or parotid glands. Although Sjögren[5] recorded the necropsy findings in one case in 1933, B. C. Cardell and K. J. Gurling[14] could find by 1954 no more than seven single case reports in the literature, to which they added three. They concluded that Sjögren's syndrome was a distinct entity characterized by widespread degenerative and atrophic changes in the conjunctivae, lacrimal and salivary glands, and the submucous glands of the respiratory and upper alimentary tracts, with secondary changes in the particular mucous membranes; and they were impressed by the resemblance of the histological changes in the affected glands to certain non-inflammatory lesions of the thyroid. In the early stages lymphocytic infiltration predominates, giving way after a number of years to parenchymal atrophy and replacement with fibro-adipose tissue containing peculiar epithelial islets. It is worth noting that evidence of polyarteritis nodosa was found in 2 of the 10 cases examined at necropsy. Those with the urge to classify may with some justification place Sjögren's syndrome with rheumatoid arthritis among the diseases of collagen; but this does little to increase our knowledge of this strange and unpleasant disease.

Air Vice-Marshal P. B. Lee Potter has been appointed Director-General of the R.A.F. Medical Services from February, 1957, in succession to Air Marshal Sir James Kilpatrick.

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[2] Thompson, M., and Eadie, S., *Ann. rheum. Dis.*, 1956, **15**, 21.
[3] Gougerot, H., *Bull. méd.* (*Paris*), 1926, **40**, 360.
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[5] Sjögren, H., *Acta ophthal.* (*Kbh.*), 1933, suppl. 2.
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[11] Reader, S. R., White, H. M., and Elmes, P. C., ibid., 1951, **10**, 288.
[12] Gurling, K. J., ibid., 1953, **12**, 212.
[13] Collins, D. H., *Rep. chron. Rheum. dis.*, 1937, **3**, 49.
[14] Cardell, B. S., and Gurling, K. J., *J. Path. Bact.*, 1954, **68**, 137.

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How severe a gastric irritant is aspirin?

FURTHER RESEARCH has now been done into the irritant effects of aspirin upon the gastric mucosa. A detailed report on this work appears under the heading "Aspirin and Ulcer" in the B.M.J., July 2, 1955.

The summary of the discussion appended to this report is as follows:

"Aspirin is a serious gastric irritant, particularly in peptic ulcer patients."

Here is a further extract from the report: "In conclusion it is suggested that aspirin should never be given to patients with peptic ulceration, or indeed to those who have any gastric intolerance to it, however mild. Such an instruction should be given a prominent place in peptic ulcer advice charts, usually in place of much that could be safely left out. Some of these patients took aspirin on a full stomach only in powder form. with serious results, and, although this method almost certainly mitigates its irritant effects, it does not guarantee immunity. Calcium aspirin does not have this irritant action unless it has deteriorated through standing, and it can be used with impunity, especially if prescribed in soluble form. This simple measure would, in our opinion, cut down significantly the incidence of haematemesis and exacerbations of ulcer symptoms."

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12

SOME PRINCIPLES AND METHODS OF INTERNATIONAL HEALTH WORK

BY

H. S. GEAR, M.D., D.P.H., D.T.M.&H.
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Increasing numbers of the medical and related professions of all countries are taking part in the work of the World Health Organization. They do so as W.H.O. consultants and advisers to the large number of countries which seek assistance from the Organization; as members of W.H.O. panels and committees giving the necessary technical guidance to the Organization; as contributors of technical information; and as members of the large number of national institutions contributing to world services concerning epidemiology, health statistics, therapeutic substances, medical education, communicable diseases, and many other subjects.

This relationship is different from that of the full regular staff members. It is also a much more comprehensive relationship. At December 31, 1955, for example, W.H.O. had 152 medical and related scientists on its regular staff. These occupied mostly medical and technical administrative posts, as the Organization does not have its own clinical, laboratory, or other medical institutes. On the other hand, at the same date W.H.O. was using 295 senior consultants, advisers, and demonstrators in 63 countries and territories, and during 1955 appointed 59 specialists to serve on eight of its expert committees. In addition, large numbers of medical and other associated scientists from the majority of countries attended a variety of meetings, conferences, seminars, study groups, etc., sponsored by the Organization. There were representatives from every branch of medicine—clinical, institutional, laboratory, and administrative. Such a relatively large number of medical people helping W.H.O. each year makes some of its arrangements and methods especially important to the medical and related professions.

Constitution of W.H.O.

There is no need here to give the history of international health co-operation or to consider the detail of the W.H.O. constitution or organization. Much of this has been given previously in the *British Medical Journal*.[1] It is perhaps enough to say that the overwhelming need for an international health body developed not only from medical but also from welfare, social, and economic requirements in all countries. The consequent formal association of countries already has a history of over a hundred years, of which W.H.O. is the present expression.

The countries of the world created W.H.O. to do on their behalf such things as providing appropriate international health services; giving technical information and counsel; assisting governments to meet their health needs; and, of especial importance in view of events, co-ordinating international health work. Arrangements were made for universal membership of States. To-day, with 81 Member States and four Associate Members, such universality has almost been obtained (though a certain few governments do not take an active part). The governments also authorized the basis for W.H.O.'s administration, including authorities for staff, finance, regionalization, and relations with other organizations.

It is in the Constitution that the principles are found which explain the arrangements and methods used by W.H.O. The Constitution is itself based on the concept of an association of sovereign States. If this principle is constantly recalled, the way W.H.O. works will usually be understood. Put conversely, W.H.O. is not a form of supranational organization. As Mr. Hammarskjold, the Secretary-General of U.N., put it at the Pilgrims' Dinner in London on March 18, 1954, when referring to the United Nations: "We need to think of the institutions of the United Nations not as parliamentary in character but as a framework within which the Governments can, by trial and error, build up traditions of world community. . . ."

The important consequence of this is often overlooked—namely, that an international organization like W.H.O. does not itself directly control or undertake medical and health programmes in countries. It is the national services assisted by W.H.O. that give effect to the field programmes adopted by the World Health Assembly.

Nature of the Organization

The Constitution provides for an intergovernmental policy-making organ—the World Health Assembly. This has an Executive Board of eighteen individuals designated by as many governments, and there is then an administrative machine—the Secretariat—to carry out the instructions of the policy-making bodies. The constitutional character, and the developing mode of operation of these two, the Assembly and the Board, are themselves worthy of study, but for present purposes one emphasis is required. The World Health Assembly is a meeting of governments. It is not a gathering of medical men in a professional congress or conference. It is essential, therefore, and quite legitimate, for the Health Assembly in establishing international health programmes to take note of many factors—economic, administrative, and even political—which a purely medical or technical meeting could perhaps ignore. As W.H.O. is an intergovernmental and not a supragovernmental body its resolutions are normally recommendations to governments for action. It is to be noted, with a few specific exceptions, that even the decisions of the Health Assembly are not automatically binding on governments.

The Secretariat, headed by the Director-General, operates in and from seven offices—the Headquarters in Geneva and the six Regional Offices: temporarily in Geneva (presently to be in Copenhagen) for Europe; Washington, D.C., for the Americas; Manila for the Western Pacific; New Delhi for South-East Asia; Alexandria for the Eastern Mediterranean; and Brazzaville for Africa. The Secretariat is an international civil service. It is not a policy-making body, and it is not its own master.

These are further facts which, if always remembered, would simplify understanding and avoid frustrations among some medical and technical groups associated with W.H.O. It is the governments, not the Secretariat, which prescribe policies, define programmes, and provide the means. However, the young international public service which exists in W.H.O. can claim to have something of the nature of such a national civil service accorded the descriptions: "Permanent, Independent and Influential," and ". . . . Growth without Bureaucracy."[2]

It is permanent in the sense that it does not come and go with annual decisions of the Health Assembly. It is independent in its constitutional obligations, set out in Article 35 of the Constitution:

> "The paramount consideration in the employment of the staff shall be to assure that the efficiency, integrity and internationally representative character of the Secretariat shall be maintained at the highest level,"

and further elaborated in Article 37:

> "In the performance of their duties the Director-General and the staff shall not seek or receive instructions from any Government or from any authority external to the Organization. They shall refrain from

[1] *British Medical Journal*, 1950, **1**, 1021-51.

[2] The British Civil Service, *The Times*, November 23 and 26, 1953.

any action which might reflect on their position as international officers. Each Member (that is, Member State) of the Organization on its part undertakes to respect the exclusively international character of the Director-General and the staff and not to seek to influence them."

In that the W.H.O. Secretariat is not a direct operative civil service it cannot have a direct type of "influence." However, apart from the opportunity for "influence" which follows respect for the honesty and efficiency of any service, the W.H.O. Secretariat has several significant formal rights. For example, Article 32 of the Constitution says: "The Director-General shall be the *ex-officio* Secretary of the Health Assembly, of the Board, of all commissions and committees of the Organization and of conferences convened by it." Further, the Director-General may make proposals for the agendas of the Health Assembly and the Executive Board, and, apart from formal reports to these bodies, he may make statements, oral or written, before them.

A frequent misunderstanding would be avoided if another constitutional provision was remembered. Article 71 reads:

> "The Organization may, on matters within its competence, make suitable arrangements for consultation and co-operation with non-governmental international organizations and, with the consent of the Government concerned, with national organizations, governmental or non-governmental."

This contains a remarkable principle pregnant with opportunity. It means that W.H.O. is not limited to "official" interests only, important though these are. It has been given the privilege of associating both official and non-official organizations in international health and medicine. In W.H.O. the professional, medical, and other similar groups of the world, through both their international and their national associations, take their essential part. Thus they may have a direct say, under certain conditions in the governing bodies—the World Health Assembly and the Executive Board—in influencing major policy and administration. This is in addition to the contributions they make to the technical arrangements of the Organization. Such international medical professional bodies as the World Medical Association, International Association of Microbiological Societies, World Federation of Mental Health, International Unions against Cancer, Tuberculosis, and Venereal Diseases, International Dental Federation, International Council of Nurses, and many others in medical, social, and health fields are associated with W.H.O. in this way. To take one example only, the World Medical Association has greatly assisted W.H.O. by its authoritative guidance on a variety of subjects, including industrial medicine, pharmacopoeias, and medical education.

The basically advisory nature of W.H.O.'s relationship with governments on the operative side in connexion with the execution of programmes is one safeguard against some bureaucratic faults. Generally W.H.O. may not exercise central administrative control of, nor direct or supervise, local country activities. It has no right to interfere in any way in the internal affairs of any country or community. There are, however, other tests of the absence of bureaucracy, and these too, I think, can be met.

Some W.H.O. Policies

The work of W.H.O. may be conveniently divided into its direct advisory services to governments requesting assistance, and into certain technical services of general international interest, though there is inevitably an overlap on occasions. In the first group are the projects in most countries covering practically the whole range of public health and medicine. Yaws control in Haiti and the Philippines; trachoma studies in Iran and North Borneo; advice on medical administration in Burma and Panama; nutrition surveys in Brazil and Indonesia; maternal and child health in India and Thailand; assistance to nursing schools in Malaya and Syria; are examples of these services. At December 31, 1955, there were 218 such programmes in 63 countries and territories being assisted by W.H.O. It is these programmes which at present are of most interest to the medical and other professions, as it is to work in them that most of the consultants and advisers come to serve W.H.O. for short periods.

Certain policies governing these advisory services may therefore be usefully discussed because of their general professional interest. W.H.O. operates a project only on the request of a government, and only by providing assistance to the government. For example, a country desiring help to develop a programme of venereal diseases control submits a request to W.H.O. The consultants sent out by W.H.O. then work by advising and assisting the local services. They do not establish a separate W.H.O. venereal diseases service in the country.

Governments retain entirely the right to express their own wishes regarding the type of international health assistance they desire. This partly explains the disappearance of the original "priorities" established by the First World Health Assembly in 1948. Planning at that early stage being unavoidably somewhat academic, the Assembly had prepared a world programme giving priority to six subjects: malaria, maternal and child health, tuberculosis, venereal diseases, nutrition, and environmental sanitation. Further, countries have increasingly extended their requests to cover integrated health and medical services rather than to limit them to the isolated subjects of the "priorities." To-day, therefore, these "priorities" can no longer be followed in developing the advisory services. However, the Health Assembly and Executive Board have defined certain principles in the selection of requests. Some of these have become fundamental not only in W.H.O. but in many other international organizations when giving technical assistance to governments.

One of these principles is now almost enshrined as a philosophy in all work where governments receive assistance. It is that projects should be designed "to strengthen national health administrations." This may sound like a simple platitudinous phrase. It is not. In the earlier years some people argued that W.H.O. should meet government requests by itself dealing directly with the particular local problems. For example, using this latter method to help a malarious population, W.H.O. would go in and develop its own *ad hoc* malarial organization and conduct a direct anti-malaria campaign. This call for direct so-called practical action had, understandably, much appeal.

However, the importance of self-help and local responsibility; the avoidance of extreme centralization of direction and technical planning, and of remote control; the need to adapt medical arrangements to local social and economic circumstances, and to resist the creation of a large permanent international civil service, were amongst the compelling arguments against the system. These, added to the recognition of national sovereignty, determined the policy that W.H.O. should assist countries by "strengthening national health administrations." This bald statement of the policy has occasionally been misinterpreted. It does not mean that W.H.O. services are available only to a central official governmental service. They can provide assistance through governments to any form of institution, organization, or service fitting into the local pattern. It is fortunate that an early Assembly took a decision to adopt this fundamental principle, which is sound administratively and in harmony with most accepted views on good public health and medical practice.

The abandonment by the Health Assembly of "priorities" has not meant rejection of the need for W.H.O.'s assistance to be distributed sensibly. The Health Assembly and Executive Board require some tests to be applied in both the Central and the Regional Organizations before acceptance of projects. Such criteria[1] to be met include, in general terms: international feasibility and acceptability; benefit to the largest possible number of Member States and people; availability of qualified person-

[1] *Off. Rec. Wld Hlth Org.*, 1951, **32**, 55-63.

nel; preliminary studies and preparations have been made; the ability of the national government to continue and complete the work; full account has been taken of related possibilities of financing and action by other agencies and integration with related projects; and financial feasibility.

Vague though the language of some of these criteria may be, there is enough indication of several important principles to be followed. In the preliminary stages of negotiation on programmes between W.H.O. regional directors and governments and of discussion at the regional committees, some classification of government medical requests thus becomes feasible. Patently unsuitable projects are now rejected—indeed, are being less frequently presented. A country suffering heavy mortality and morbidity from more easily preventable conditions for which "outside" technical assistance is suitable is now not likely to demand as more urgent an electron microscope or a highly specialized hospital.

In certain regions the development of "country projects" is now following a pattern of study and application. An identified health problem often first needs examination internationally by a study group, by one or more experts visiting several countries concerned in the matter, or by simultaneous and co-ordinated studies in selected countries, before methods of dealing with it can be determined. The results of such an examination can then be disseminated on a wider basis through seminars, conferences, symposia. From this phase there often emerges a need for a new type of training suitable to be organized on an inter-country basis where controlled experiments can be arranged on new curricula, team training, etc.

Another general policy influencing the system of advisory services to governments is for W.H.O. to support the training of medical and health workers. This purpose is met in two general ways. Firstly, by a system of international W.H.O. fellowships, and, secondly, by helping countries to establish or improve their own medical training institutions. These two methods, owing much to earlier international experience, have combined to give W.H.O.'s programme of professional and technical education both success and popularity. In 1955 W.H.O. provided 1,028 fellowships, almost all postgraduate. The fellows came from 108 countries and territories and visited 75 countries and territories to receive their training. In keeping with the principle of "strengthening national health services," W.H.O. fellows are obliged to return for a minimum period of three years' service in their own country.

A significant feature of this international medical policy is that both "receiving" and "giving" countries and their medical professions contribute and benefit. A country like the United Kingdom, through W.H.O., is each year the source of numbers of senior medical teachers from its leading universities, who go to other countries to assist the development of their medical faculties and training institutions. Conversely, the well-known institutions of the United Kingdom, also through W.H.O., in 1955 gave advanced training in all branches of medicine to 206 doctors and scientists from other countries. Here, indeed, is a mutually beneficial process both to the countries sending fellows and receiving consultants and to the United Kingdom in having its institutions linked with developments in many countries. It extends, too, good will and even material advantage far beyond strictly medical circles.

A further expression of the various principles mentioned above is that W.H.O. does not possess its own medical institutions or operative medical services. Reference is not intended here to the long-established and accepted general international services connected with epidemiological and health statistical reporting, biological standardization, and other similar subjects, but to the fact that W.H.O. does not have its own hospitals, field medical services, or research institutions. This policy is an expression of the view that variety, freedom, and elasticity of conditions are needed by science and medicine in both investigation and application. These are more likely to be found in a number of different country institutions than in a centralized uniform official organization.

This method of working through the institutions of others is sometimes misunderstood by medical and other scientists, individualistic by training and experience. Accustomed to work in the laboratory, at the bedside, or in the field directly on their own programmes, the change to the more detached role of adviser or of medical administrator is often disturbing. It is a further facet of the position of indirect relationship, mentioned above, which W.H.O. has with its constituent governments which, once realized, enables suitable adjustment by the staff to be possible in most cases.

Co-operative Arrangements

Co-operation, co-ordination, and integration are words of common currency, if not yet debased to jargon, in international life. Yet they have more urgency and importance than in national operations. If international work is to mean anything, then co-operation and co-ordination are fundamental principles. To ignore their importance leads to inefficiency, waste, and even the disrepute of the concept of governments working harmoniously together through the existing system of international agencies. This is certainly true of international health work. The W.H.O. Constitution and numbers of policy decisions of the World Health Assembly and the Executive Board emphasize the development of all programmes by co-operation with all other interested agencies, and their integration into associated arrangements, international and national.

Achievement of the ideal is not yet here. There are the difficulties in co-ordination of work by the various international administrations themselves, with interests overlapping in many places. Interdepartmental and inter-organizational problems are not peculiar to national services. Indeed, the interests to be reconciled are more numerous.

In actual country work the problems for international agencies of co-ordination and integration are accentuated. Each agency can achieve there no more and no less than the authority and administration of the local government provides. Each faces, too, the additional complexity that there are usually other international agencies assisting the same government in related fields of work.

A disease control programme, for example, can be influenced by decisions taken by: (*a*) the United Nations General Assembly, the Economic and Social Council, the Technical Assistance Committee, the World Health Assembly, the Food and Agriculture Conference, and others; (*b*) the executive organs of the various agencies; and (*c*) the numerous national bodies concerned in local administration, agriculture, labour, health, etc.

This complex background to health work gives the principle of co-operation and co-ordination its importance. It calls for negotiation, adjustment, and considerable compromise before international health programmes are planned, provided for, and finally undertaken. Qualities of diplomacy, persistence, tolerance, and patience are required in the staff of the Organization to a greater extent perhaps than in any national situation.

One of the lessons, perhaps hesitantly learned by many medical men accepting the role of advisers to governments, is that more "medicine" is not necessarily the most urgently desirable step to improve general health. The dependence of community health on economic, social, and political interplay, in which more hospitals, clinics, and medical specialists do not always figure prominently, is sometimes hard for doctors to acknowledge. Then, too, it is sometimes unpalatable to accept the view that the cost of health should be measured against other claims. This need, described for instance by Ffrangcon Roberts in the *British Medical Journal* and elsewhere,[4] is occasionally overlooked in situations where national resources are limited. It is forgotten that the application of medicine is not outside economic laws.

Nevertheless, in all governmental developments—social, economic, industrial, or agricultural—medical advice is essential to put standards of living on a sound, durable basis.

[4] *The Cost of Health*, 1952. Turnstile Press, London.

Though sometimes he may be denied his hope of medical institutions being immediately established, the medical adviser has yet an important role in international assistance to all types of country. Often he will be helping the cause of health more by giving medical advice in relation to an agricultural scheme or an industrial enterprise than by limiting himself to a purely medical institutional programme.

Some Administrative Arrangements

There are many other policies influencing type and method of work, but only one more is selected for reference here. Article 35 of the Constitution, mentioned above, gives the importance of efficiency and integrity of the staff, but it further says: "Due regard shall be paid also to the importance of recruiting the staff on as wide a geographical basis as possible." The problem of securing geographical distribution in origin of staff has been a recurring problem for all intergovernmental agencies. The League of Nations found that "a decision to think only of building an efficient staff and to let the blows to national *amour-propre* fall where they may, would be defensible in theory. But the results would be serious. A system which depends upon the co-operation of Member States cannot ignore the factor of national prestige and interest."[4]

A regular staff originating from a single region and culture and/or with technical experience in certain "advanced" countries only, could not sponsor successfully a world-wide health and medical programme in which adaptation to local needs and co-operation with innumerable national and social groups are fundamental. It is fortunate, therefore, that the arrangements for the advisory technical staffs on the one hand, and the regular form of appointment for the central and regional administrations on the other, provide elasticity. This helps to satisfy the call for wide geographical distribution without necessarily neglecting technical standards in recruiting staff. Results of recruitment have to bear analysis by national delegations, diplomatic services, country administrations, and, perhaps the most important, by the medical and scientific professions of the world. Whether the technical standards and achievements of W.H.O., dependent upon the ability and skill of its staff, merit respect, will be judged by the medical groups of all countries.

Constitutions and policies are ultimately revealed in administrative action. Much of this outcome has been given above, but certain other administrative methods are selected for examination.

There is the type of public service created by W.H.O. to carry out its work. Several of the facts about it have been mentioned. It is already clear that W.H.O. does *not* have a large centralized force of permanent officials, doctors, sanitarians, nurses, laboratory people, and their administrative and clerical assistants. The intention of its constitution and of its legislative authority to advise governments, and not to assume supragovernmental status, is secured through two groups. Firstly, there is the regular staff who, as already indicated, perform the essential continuing technical and administrative functions and who assist in providing certain advisory and "permanent" general technical services. Then, secondly, as also previously mentioned, there is a large specially recruited technical staff to give direct assistance to governments. While they are on W.H.O. projects these people are under its general service code, which naturally requires, *inter alia*, observance of objectivity, and loyalty to the Organization.

The use of temporary and not "permanent" staff in this work has certain advantages. The technical problems vary from year to year and some conditions are unlikely to require continuing W.H.O. assistance. Only a very large permanent technical staff could meet such continually changing demands. Further, W.H.O.'s indirect method of work would mean almost insuperable difficulty in a truly "permanent" staff retaining a specialized technical skill. An "expert" can continue as such only by constant direct practice in his special work.

Specially recruited staff, on the other hand, enables W.H.O. to seek the best available adviser for each particular local problem, to adjust country technical staff continuously to the needs of the moment, to avoid staff redundancy when programmes end, and to guard against an international organization depriving national services permanently of their own essential technical staff. In practice, most consultants and advisers have adjusted themselves well as international officers in new spheres of work. This type of service indeed enriches all concerned—the "receiving" and "giving" countries, the "expert," and W.H.O.

There is another extensive arrangement by which W.H.O. draws on the technical resources of the world. This is the wide use of expert advisory panels and committees. The Health Assembly and Executive Board rely on such bodies for the general technical guidance needed to prepare programme policy. Serving on them are large numbers of the world's eminent medical scientists and health administrators in the W.H.O. fields of work. This expert panel and committee system has considerable advantages. Again, W.H.O. is able to draw quickly, efficiently, and economically on the best skills and knowledge required for the problems of the moment. It has its technical policies governed by a wide range of experience and knowledge, unlikely to be concentrated in a permanent official full-time staff. These advantages, generally, more than balance certain well-recognized weaknesses of the committee system in technical subjects.

On the whole the W.H.O. expert committees are forming a suitable instrument for their purpose. They have provided the scientific guidance and stimulus for the adoption of the international health statistical nomenclatures, international sanitary regulations, pharmacopoeia, and biological standards. They too have advised the Organization on public health, clinical and laboratory aspects of tuberculosis, child health, nutrition, malaria, and many other subjects.

The expert opinion, whether from the panel, committee, or individual, is integrated into W.H.O. programmes by the Executive Board and the Director-General. The fact that the full views of the expert are not automatically endorsed is occasionally questioned. Quite naturally the expert does not always accept happily a decision allotting more weight to other than technical considerations. But any organization concerned in problems with political, economic, administrative, as well as technical features, is obviously unable on occasion to adopt immediately all the desirable proposals put to it.

Numerous medical institutions in many countries are linked with W.H.O. There are long-established international centres, such as those at London and Copenhagen holding the accepted international biological standards, the influenza centres in London and Washington linked with a world-wide network, and others in health statistics, virus, blood work, and a variety of subjects.

Relatively small money grants are the material contribution that W.H.O. makes to such centres—a contribution which in no way measures the valuable two-way interchange that occurs. On the one hand, through W.H.O. countries everywhere draw on the resources of the central system, with many medical, economic, and industrial advantages. On the other hand, medical institutions and professions of an increasing number of countries become active partners with W.H.O., thereby contributing and gaining many things.

Many critics, especially such individualists as medical men, will wonder if W.H.O. can avoid the more serious evils of over-organization and over-administration. They will think with Sir J. F. Wolfenden, Vice-Chancellor of the University of Reading, that "a cure must be found for the modern scourge of 'organization.'"[5]

[4] *The International Secretariat of the Future*, p. 22, 1944. The Royal Institute of International Affairs, London.

[5] Wolfenden, J. F.—Address to Conference of Education Association, London, January 3, 1952.

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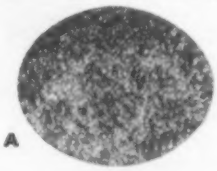

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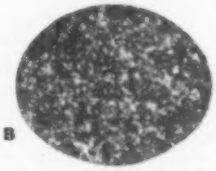

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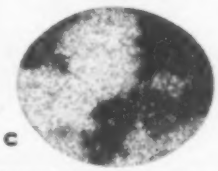

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Bureaucratic Risks

Some of the answers have been given in this article when the Constitution and legislative policies were quoted as a protection against W.H.O. becoming an exaggerated, ever-expanding international civil service, busying itself with too much detail. However, there are bureaucratic risks. Meetings—legislative, expert, or liaison—are multiplying in international work, and correspondingly absorb staff, time, energy, and money. Meetings there must obviously be in any representative organization, but when does their number cause too much diversion from progressive work? A round of meetings, tours, and reports in national or international life too easily becomes an end instead of a means.

The meetings involving W.H.O. are only to a limited extent under the control of the Secretariat. Through its obligations and agreements W.H.O. must send representatives to numbers of both international and national meetings. To decline invitations is also too often a cause of aggrievement. Thus the Secretariat itself is restricted in its power to control meetings and travel. This must largely come from the Member States of the various international organizations themselves.

Another administrative element exposed to bureaucratic exaggeration is the production of reports and documents. As Jules Romains puts it : "The peculiar symptom that betrays the bureaucrat is an unslakable thirst for paper." Paper now pours forth in both national and international work—reports, publications, questionaries, documents, and working papers. Many services use much of their time and energy merely to read and initial correctly this volume of paper. Again, the best administrator, not to be confused with the bureaucrat, desiring to treat paper as but a means to an end, can himself only partly cut off the flow. Much of it is demanded by assemblies, conferences, and committees, which it is his duty to serve. This could become an insidious evil if governing bodies and their servants accepted the report as the completion of a task instead of an item to reach that end.

This is but one of the many problems the modern organized world has in dealing with the method of communication. Much of the recent examination made by the University of London of the difficulties of communication applies to an international form of organization. A relevant example from this study is where Sir Geoffrey Vickers says : "The transmission of information is limited in the first place by logistics. The sender is absolutely limited by what the receiver can absorb in the time which he can spare from action. Volumes of paper which are circulated 'for information' are pulped without ever informing those for whom they were chiefly intended, simply because these recipients did not have or make time to read them."[1]

The Executive Board of W.H.O. has been conscious of the obstruction to purposeful work of excessive meetings, travel, and paper. These problems, too, are under continuous scrutiny by the staff. This vigilance is to some extent the assurance that such flowerings of bureaucracy will be regularly pruned.

Medical and other scientists coming to work directly or indirectly with W.H.O. will perhaps find one administrative principle particularly reassuring. It is that the Secretariat operates on a basis of delegation of responsibility. The individual units manage their own affairs with the minimum of interference from others. The technical officers and groups are free, too, in their respective technical fields. Their proposals, translated to the administrative sphere, may be subject to administrative and financial influences, but intrinsic scientific and technical data and opinions are protected.

Conclusion

This brief account has but superficially given some of the main elements determining the methods of work of W.H.O. likely to interest the medical and similar professions. These circumstances explain both the limitations and the opportunities of those doctors and scientists from all countries assisting the Organization on its regular or temporary staffs. They cannot always have the full satisfaction of following all their own inclinations in what they do, nor of running their own institutions, nor of ignoring elements they may dislike.

They do have the reward of playing a worthy part in giving of their technical and human knowledge and skill to assist mankind everywhere ; of joining with colleagues of all countries in the extension and diffusion of medical experience ; and of presenting and advocating the cause of medicine in the international and intergovernmental counsels of the world. Perhaps no other group has such opportunity, indeed responsibility, for showing the possibilities for good in international association and work. Here is an important way to the inherent universality of the science and humanitarianism of medicine.

[1] Vickers, Sir G., *Studies in Communication*, p. 82, 1955. Martin Secker and Warburg, London.

SYMPOSIUM ON ARTERIOSCLEROSIS

[FROM A SPECIAL CORRESPONDENT]

A conference on arteriosclerosis organized by the Swiss Academy of Medical Sciences was held in Basle from August 8 to 10. The president of the Academy, Professor A. GIGON, invited to the meeting research workers from 10 countries and 4 continents who are actively engaged in problems associated with arteriosclerosis.

Professor GIGON, opening the proceedings, outlined the basic idea behind the symposium. The programme was divided into two major sections. The first day was devoted to papers on blood vessel factors and arteriosclerosis, including all generalizations on morphological changes in the vessel walls and problems on the haemodynamics of the coronary system, and so on ; these subjects were considered in a series of 10 papers. The second and third days were occupied by a series of 26 papers on the problems of metabolism and arteriosclerosis. This rather wide category was further subdivided into three sections—the blood lipids and lipoproteins, dietetic factors in arteriosclerosis, and hormonal factors in arteriosclerosis. The conference was completed by a discussion on the papers and additional discussion on the problem in general.

Professor Gigon explained that Professor G. Lyman Duff (Montreal) was to have presented the opening paper under the title of "A Survey of Recent Experimental Investigations of Arteriosclerosis," but with regret he had to announce that Professor Duff was unable to be present. Consequently he called upon Professor WILLIAM DOCK (New York) to give the opening lecture.

Problems Outlined

Professor DOCK, who had originally been scheduled to speak towards the end of the congress, chose for his lecture the provocative title "Are There Effective Ways of Managing Arteriosclerosis ?" In a spirited address he made it quite clear at the outset that the answer to this question at the present time appeared to be definitely in the negative. He quickly gave a skilful outline of the many morphological and metabolic problems which confront the investigator in the field of arteriosclerosis, and drew attention to the anatomical difference which exists between the intima of the newborn male infant compared with the female infant as one possible factor predisposing the male to coronary atherogenesis. The well-known sex difference in the incidence of the clinical presentation of this disease between males and females in the white population was reviewed by the speaker, and he commented on the loss of immunity by females after the menopause. Professor Dock went on to say that one of the most striking results in the field of sex hormones in

relationship to coronary artery disease had been the observations of W. S. Bauld and associates in Montreal, who had demonstrated that the metabolism of oestradiol-17 β was different in normal healthy males compared with males of the same age suffering from coronary artery disease.

The speaker then went on to the subject of diet and disease, and commented (without reference to the source of the information) upon the very high incidence of coronary deaths among young males called up for national service with the United States Forces. It appeared that this section of the American population is required to consume vast quantities of butter, cream, eggs, and animal fat during their military service, and Professor Dock implied that this parameter required immediate investigation. The possible role of cigarette smoking and the differences which appear to exist between the incidence of certain forms of arteriosclerosis in communities who ingest animal fats and the incidence in communities who ingest largely vegetable fats were very briefly mentioned. The speaker concluded by contrasting the economics of prescribing a diet designed to lower the serum cholesterol against the cost of the so-called hypocholesterolaemic drugs, and said that the patient nowadays required education in the cholesterol content of various foods and the cholesterol content of his own tissues. Thus he hoped that a return to a diet "normal for man" might be the method of choice of the Hippocratic physician.

Morphology

Among the many interesting papers presented in the period devoted to morphological studies was a communication delivered by Dr. P. COHRS (Hanover), who focused attention on the fact that the parrot exhibits spontaneously a type of atherosclerosis which is similar in appearance and distribution to that prevailing in man. The birds studied by the speaker varied a great deal in age, and some were known to be older than 30 years. The diets were of course uncontrolled, but it did seem to your correspondent that the parrot might have a useful place in investigations of this type, since the lesions were more closely related to those found in the human than those occurring in the lipoidoses in other birds such as ostriches and turkeys.

Professor A. MÜLLER (Fribourg) gave an authoritative account of some of his studies on the haemodynamics of the coronary system. He developed the mathematical arguments in favour of a sort of backward shock wave from the periphery towards the aorta, which leads to changes in the velocity of the blood in the coronary system of the order of 50–60 cm./0.2 sec. Professor Müller showed that the consequences of these effects would be most apparent at positions further removed from laminar flow, and this would be at the bends in the coronary system.

Professor J. B. DUGUID (Newcastle) put to the meeting in a concise manner his general thesis that the process which causes narrowing of the arterial system is not fatty change but thrombosis. This speaker went on to say that there were all types of thrombi, from the large type which filled the lumen down to small wisps of fibrin attached to the intima. The fibrin masses were often to be found covered by a layer of endothelium, and Professor Duguid concluded that thrombosis does not necessarily depend on fatty changes in the arteries, as in his view the fatty changes are the result, rather than the cause, of thrombosis. He emphasized that pathologists must differentiate between lesions which are primary fatty changes and secondary fatty changes seen after thrombosis.

Metabolic Factors

In the metabolism section of the congress Dr. F. T. LINDGREN (Berkeley) discussed the relationship of the blood lipids and lipoproteins and coronary disease. The plasma lipids are almost solely in the form of lipoproteins, and the author gave the chemical analysis of some of the low density lipoproteins. From studies which Dr. Lindgren had made as a member of Dr. Gofman's group in California, he presented data to support the argument that the rate of development of arteriosclerosis can be calculated from ultracentrifugal analysis of the low and high density serum lipoproteins, and this information was computed into an "atherogenic index." It was shown that this index was higher in individuals with angina who went on to myocardial infarction than in another group who had angina only. It was shown that the atherogenic index was lowered by the administration of heparin or desiccated thyroid and also by the consumption of a low fat diet. The speaker concluded that, when an ultracentrifuge was not available, serum cholesterol studies should be combined with concurrent serum total lipid determinations in order to obtain maximum information.

Professor A. FASOLI (Milan) delivered an interesting paper on a study which he had made of the filter paper electrophoresis method of lipoprotein assay, contrasting this with the ultracentrifugal method. Professor Fasoli showed that the electrophoretically determined alpha : beta lipoprotein ratio must always be interpreted with great caution, as he had observed considerable variation in both normal and pathological serum samples.

Professor G. SCHETTLER (Marburg) showed that in several patients who appeared to be mildly hypercholesterolaemic a diet of about 1,000 calories daily for about 10 days produced a fall in the serum cholesterol of approximately 30%. He went on to discuss the effect of the unsaturated fatty acids in lowering the serum cholesterol, and concluded that a low fat diet and/or caloric restriction may be desirable in subjects who present with hypercholesterolaemia, but persistence over a long period would be required in order to establish the usefulness of this regime. This paper was followed by a similar contribution by Professor H. MALMROS (Lund), who also showed that vegetable fats lowered the serum cholesterol and mentioned that this effect was independent of the cholesterol content of the foodstuffs. Professor Malmros presented some of the results which he obtained in association with Professor A. Keys (Minneapolis) in which the serum cholesterol values of clerks, foremen, and heavy workers in Malmö, Sweden, were compared with similar workers in Naples, Italy; the Neapolitans were all significantly lower than the Swedes. Professor Malmros urged that only well-characterized acids should be employed in all studies on the effect of the so-called "essential fatty acids" on the serum cholesterol. He showed that the incorporation of these unsaturated fatty acids into a normal diet could keep the serum cholesterol down for periods up to six months in certain selected cases.

Alpha and Beta Lipoproteins

Professor D. P. BARR (New York) gave a review of some of the studies performed by his group, utilizing the modified Cohn fractionation procedure to derive the distribution of cholesterol between the alpha and beta lipoproteins of serum. The author pointed out the statistically significant difference which exists between the serum of normal young women and normal young men, the latter having less cholesterol bound to the alpha lipoprotein than the former. This sex difference completely disappeared in older "normal" subjects, but males or females with coronary artery disease always had a lower alpha : beta ratio than had "normal" subjects of comparable age. Professor Barr went on to show that the administration of 1 mg. of ethinyl oestradiol daily to subjects with abnormal lipoprotein patterns, such as occur in xanthomatous cases, coronary artery disease cases, cretins, and in cases of myxoedema, always resulted in the serum lipoproteins shifting towards normality.

Dr. G. S. BOYD (Edinburgh) reported that the administration of small doses of triiodothyronine and triiodothyroacetic acid could result in depression of the serum cholesterol without influencing the basal metabolic rates of the subjects, but larger doses of these drugs overcame this dissociated action with a resultant rise in the B.M.R. Speaking

on behalf of the Edinburgh group, Dr. Boyd suggested that caution was required in the use of these substances as hypocholesterolaemic agents because of the considerable variation in individual dose response—a decreased exercise tolerance was observed in some cases—but the substances seemed to merit a fuller clinical trial.

This report details only a fraction of the material presented to the conference, and many excellent papers have not been mentioned. However, your correspondent was struck by the lack of really new material presented; in fact, opinions on arteriosclerosis appeared to be in a phase of active consolidation on both the morphological and metabolic aspects of the disease. Perhaps before the next major meeting on the subject there may have evolved newer, and doubtless more expensive, methods designed to unravel this affliction of mankind.

Nevertheless, the meeting was most successful and instrumental in bringing together investigators who would otherwise know one another only by name. The symposium was made possible through the generosity of well-known Swiss and American fine chemical manufacturers.

Nova et Vetera

ONLY EIGHTY YEARS AGO

Go back only 80 years, and in what an incredible world of medicine you find yourself! What masterly pharmacological orchestration! Come and look over the shoulder of Dr. Tschudi Madsen[1] as he peers at a tattered Prussian medical diary found hidden in the loft of a house in Bergen, the second largest town in Norway. In addition to the standard information characteristic of medical diaries, this volume had several spare pages into which a general medical practitioner, Dr. Harald Lehmann, had in 1873 crammed his medical records. He can have had no thought of ulterior publication as he jotted down his notes in a handwriting so fine that a magnifying glass is needed to decipher them. Many of his 543 patients, whose names are given, had patrician family names and were the social cream of this Hanseatic town. Their complaints? Much the same as those of 1956. But how varied the remedies for them! And how Hippocratic the differentiation of symptoms and diagnosis! For whooping-cough an infusion of tonka (from the African tonka bean). For phthisis, lichen Islandicus. For haemoptysis, salt, secale, and extractum hyoscyami. For catarrh with blood-stained sputum, cod-liver oil, rum, and milk. For asthenia, tinctura absinthi composita. For epilepsy, subcutaneous injections of ergotin in the nape of the neck. For goitre, a bag of salt on the spot every night. The versatile Lehmann took his remedies from the animal as well as from the vegetable kingdom, and he drew on the musk-ox (tinctura moschi for heart failure), the beaver, the Spanish fly (cantharides on the chest for asthma), and above all the leech. For pain in the praecordium and anywhere else, for exudative pleurisy, and for a bruised knee, always the leech. It was applied to the temples for tinnitus and for pneumonia running a fatal course. Eight leeches at a time *ad anum*. At about this time, when Lehmann was 56 years old, the sands had begun to run out for himself. He evidently referred to himself when he jotted down: "Icterus with stinking intestinal catarrh . . . lassitude . . . tar pills, tincturae aurantii and nucis vomicae, aqua regiae, and aqua ferripyrofosforici." Surely he had earned a holiday; and he took it in Italy with a small library consisting of the Bible, Baedeker, Björnson's poems, and three of Ibsen's plays. There was also a whole medicine chest. Its alphabetical list began with elixir paragoricum (good old tinct. camph. co.), and ended with vinegar. Tidy to the last, he had slipped into his medical diary a note of what he had paid for cab fares in Genoa, Naples, and Florence.

CLAUDE LILLINGSTON.

[1] *T. Norske Laegeforen.*, 1956, **76**, 120.

Correspondence

Amnion Implantation in Peripheral Vascular Disease

SIR,—The treatment of peripheral vascular disease gives no cause for complacency, and Mr. E. Troensegaard-Hansen's paper (*Journal*, August 4, p. 262) is welcome in suggesting a possible new method of treatment for patients suffering from this distressing disease. I have been carrying out this method of treatment for about the same length of time and would like to record some of my impressions.

The first twelve patients that I treated were unselected, unlike Troensegaard-Hansen's, who has limited his cases to Boyd's classifications 1 and 2. The experience with these twelve cases showed that the treatment was really only of value in Boyd's type 2; it caused no real relief to those patients who had rest as well as exercise pain, for those with incipient gangrene, and, in addition, there was no evidence of any improvement in two patients who had Raynaud's disease. The interesting fact about the patients who did improve was that the improvement was entirely subjective. I was never able to achieve any objective improvement in support of the patients' claims. On every patient the blood pressure was carefully kept, and E.C.G. was taken before and after operation, prothrombin time was similarly estimated, oscillometry and skin thermometry were also carried out, and in none of these tests were any changes noted. For the next three cases, which were all of Boyd's type 2, I carried out in addition arteriograms before and after the amniotic implants, and no alteration was seen in the arterial pattern. I realize that this is a very small number and that the test is inconstant, but I think it does denote that there is no dramatic increase in the collateral circulation.

Since Walder[1] published his paper describing a method of measuring blood flow utilizing radioactive sodium, Dr. W. Kulke, consultant radiotherapist at the Liverpool Radium Institute, has used this technique in measuring blood flow before and after amniotic implants on six cases up to the present time, and the results conform quite closely with those published by Troensegaard-Hansen. In the published graphs, however, there are some points which are subject to criticism. In the first place the patients are exercised for two minutes prior to the amniotic implant; in many of our cases the patients cannot exercise for one minute owing to the onset of pain. Secondly, the inter-exercise hump as described in Fig. 2 has not been obtained by us in any case. Thirdly, in Figs. 9 and 11, the uptake of sodium after exercise appears to be greater than before or during, which is certainly not normal, and it is difficult to assess.

Clinically, the more recent cases that I have done have been successful, and I feel that this method of treatment may well have a selected place in the treatment of intermittent claudication. I think, however, that this article should be treated as a preliminary publication. There is no direct evidence for many of the hypotheses put forward in the discussion. There is also no evidence that nucleated cells in the epithelial zone are the active part, nor is there any proof that this action is specific to amnion. Much work requires to be done in the use of living tissues in producing a similar effect—possibly another serous membrane such as pleura or peritoneum—and only time can tell whether the effect of amnion will be permanent or whether relapses will increase as the period after implantation lengthens. Like other new methods of treatment, early results may be misleading and should be treated with considerable reserve and caution.

I should like to express my gratitude to Messrs. Smith and Nephew Research Ltd. for supplies of amnion and for their constant help and encouragement.—I am, etc.,

Liverpool, 1. J. G. GOW.

REFERENCE

[1] Walder, D. N., *Clin. Sci.*, 1953, **12**, 153.

Effect of Fatty Meals on Blood Coagulability

SIR,—May I be permitted to reply to Professor H. W. Fullerton's comments (*Journal*, August 11, p. 356) on my paper (*Journal*, July 28, p. 207) on the effect of ingested fat on blood coagulation? My choice of the coronary arteries as an example of vessels commonly affected by atheroma was fortuitous: I might equally well have selected the aorta, where in fact atheroma is even more frequently found.[1] If atheroma was confined to, or even most frequently found in, the coronary vessels the unique character of the coronary blood flow might perhaps be incriminated as a necessary, if not effective, cause: but this is not the case. What Professor Fullerton does not mention is the correlation between the frequency of atheroma and the pulse pressure in various parts of the aorta. The pulse wave is greatest in the abdominal aorta, and it is here that atheroma is commonest. Yet there is no likelihood of systolic "reduction or cessation of flow" at this point which would "readily allow deposition of pre-formed fibrin" in the way he suggests as occurring in the coronary arteries as the earliest lesion of atheroma.

My main intention in repeating Professor Fullerton's experiments, using modified techniques, was to illustrate once more the importance of method in this field of research, and not to advance or repudiate a theory. However, there is one aspect of Professor Fullerton's hypothesis on which I would like to comment: it is the validity of using estimates of clotting time as a measure of blood coagulability. Under certain experimental conditions the clotting time of a specimen of blood is inversely proportional to its lipoid content. This only means that the process of coagulation has been accelerated: it does not necessarily mean that coagulation is therefore more likely to take place, as the factors which govern the speed of coagulation are quite different from those controlling its inception.

I would close by reiterating my original point: that proportionality of clotting time to lipoid content is found only in the absence of platelet activity. This does not occur in the body, and the phenomenon described is probably only a reflection of the ability of chylomicrons to imitate the action of platelets[2] and is not an indication of changes in blood "coagulability."—I am, etc.,

London, W.6. G. H. HALL.

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[1] Brooks, H., *Amer. J. med. Sci.*, 1906, **131**, 778.
[2] Cramer, W., and Pringle, H., *Quart. J. exp. Physiol.*, 1913, **6**, 1.

Benzhexol in Parkinsonism

SIR,—I was frankly amazed to read the report on a series of cases of this distressing condition by Drs. H. B. Porteous and D. N. Ross (*Journal*, July 21, p. 138), and to learn that patients were, apparently, immediately put on 7.5 mg. of benzhexol hydrochloride daily, except in the case of one aged 80. This person was only given an initial dose of 5 mg. daily.

By experience as a mere general practitioner, I am obliged to be more cautious in my dosage. I find that for sometimes a week or even more I can only prescribe one-third of a 2-mg. tablet a day, but by dint of persevering the dose can be increased to the normal 6 mg. per day, and increased after that. One fails to see why a condition so chronic, albeit progressive, should receive the full impact of high doses. In all drugs where time is more of a secondary nature, an initial low approach is surely a "must."—I am, etc.,

Tonypandy, Glam. E. B. PHILLIPS.

Maladjusted Children

SIR,—I must thank your correspondents for their support in this matter. Dr. J. G. Howells's enterprise and initiative in Ipswich (*Journal*, July 21, p. 179) are admirable, and will, I hope, encourage others to do likewise.

I appreciate that many younger graduates have had more training in child psychiatry than was customary in my youth, but my experience with young graduates is that they have little practical knowledge of how to manage a case. They usually know all about the Oedipus complex and forgot to ask whether the parents are still living together, and without a proper history remedial psychiatry is impossible. The course I had in mind for assistant medical officers of health (*Journal*, June 23, p. 1487) was of a more formal kind. Clinical lectures with actual cases are difficult to manage in the presence of more than a few students without disturbing the patient, and actual cases could be discussed in formal lectures, as well as more systematic tuition. In this way larger groups of medical officers could be instructed.

Dr. J. S. Owen's suggestion (*Journal*, July 7, p. 47) that some psychiatrists are not in favour of dilution is interesting. When I tried to persuade the late Sir James Spence that Newcastle was very backward in having no child guidance clinics, he took the opposite view. He was not at all sure that psychiatrists were the best people to treat maladjustment, or indeed mental diseases in general, and his view is shared by many physicians. We all think we understand human nature, but we must stop making jokes about psychiatrists, since this undermines patients' confidence. I suppose the reason behind the psychiatrists' objection to dilution is that a difficult case in unskilled hands may be worse after treatment. This is, of course, unanswerable, except that an important part of my training course would be the early recognition of such cases and their immediate referral to the psychiatrist. Another safe guide would be the lack of progress under treatment.

Sir David Henderson points out (*Journal*, August 27, 1955, p. 519) that of every hundred births eight will have a nervous breakdown and three of these will be of such severity as to require admission to a mental hospital, and the amount of minor illness, both purely functional and psychosomatic, which any practitioner sees is colossal. Indeed, any psychiatrist will be the first to admit that the only well-adjusted person he knows is himself.

Psychiatry has its limitations, but they are not considerable. The experience of totalitarian countries has shown how easily humanity can be conditioned, but we in the democracies have been very slow in following up Pavlov's work. Child guidance will not revolutionize our communities in a generation, but in time it can work wonders. Both Goethe and Plato, and no doubt many other philosophers, recognized the importance of the proper rearing of children for attaining an ideal state, and both considered that mothers were the last people to be entrusted with the care of their own children. While we consider to-day that mothers can be reconditioned, any psychiatrist knows how difficult it can be with the unintelligent, or the mother who cannot bear the idea that she is the cause of her child's difficulty, but even the mothers of problem families can be trained—for example, as in London, where they are housed in blocks of flats with a permanent warden, which, with other recognized aids, should be fruitful. In time the method of rearing children would become common knowledge, and then 'twill be bliss to be alive.

As I said in my last letter, I look for your support, Sir, in filling the gaps in this most important branch of medicine.—I am, etc.,

MAX PARK.

Virilism with Mental Symptoms

SIR,—The case history given below seems worthy of record because of the unusual nature of the symptoms and the fact that to-day, ten years after medical and surgical treatment ceased, the patient is fit and well.

A married woman of 25 was referred for an opinion because a profound change had taken place in her habits and attitude towards others: from being a happy and active, though shy person, she had become silent, morose, and careless in her personal habits and appearance. The deterioration came gradually following the birth of her only child three years previously. Her husband reported that she had refused all medical attention. The patient remained almost silent during the first interview and kept muttering: "Let me die, let me die." She was unkempt and there was a luxuriant growth of hair on the chin with acne and scurfy

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hair. Social conventions were disregarded, and she lounged in a chair smoking cigarettes. Beyond taking her pulse rate no examination was allowed. After several interviews the patient permitted a superficial examination. Her general condition was sound, but there was an excessive growth of hair on the abdomen and legs. Conversation was monosyllabic and it was impossible to establish any rapport. A diagnosis was made of a schizoid-depressive illness with marked endocrine disturbance.

Mr. L. R. Broster saw the patient in consultation, and he considered that her mental condition was related to an endocrine dysfunction. He advised operation, but this was declined by the patient and by her relatives. Eventually she was persuaded to enter a nursing-home, where she remained with special nurses for three months. Treatment to begin with was by E.C.T. and insulin shock, and following this she became accessible to psychotherapy. An improvement took place after two months' treatment: conversation became connected, and it was possible to gain her co-operation in the simple psychotherapy which was used. While still careless in her dress, she was tidier, and her social adaptation improved, although her mental condition was unstable and erratic. Ultimately she accepted the need for further treatment and her relatives withdrew their objection to an operation. Special examinations followed: uroselectan and *x*-ray examinations of both kidneys showed a normal function; but the shadows of both adrenals were larger than normal. She was secreting 11.9 mg. of ketosteroids daily.

Mr. Broster again saw the patient and agreed to operate. On operation it was found that both adrenal glands were enlarged; the right ovary was cystic and the left solid and without corpora lutea. The hypertrophied left adrenal—2 in. by 1 in. (5 cm. by 2.5 cm.)—was removed. Shortly after the operation the ketosteroid secretion showed a 50% reduction. The patient made an uninterrupted recovery from the operation, and after it she was able to depilate herself with satisfactory cosmetic effects. Her complexion improved, the acne disappeared, and her hair lost its scurfy appearance. There was a rapid improvement in her mental condition. For the first time in almost four years the patient undertook responsibility of a mild nature such as shopping. A notable feature was the development of initiative and the return of her sense of humour. After a few weeks' holiday she went home and resumed domestic life.

During the next two years progress was intermittent and there were relapses with a reappearance of the schizoid-depressive features and negativistic behaviour; but these symptoms cleared up without treatment. Progress since then has been steady, although the home circumstances required considerable patience and common sense. Three years ago—that is, seven years after medical treatment had terminated—the patient became pregnant, and after a normal pregnancy and confinement bore a healthy child. She is now leading a normal life, interested in her family and taking part in social activities.

The psychiatric treatment was successful up to a point, but the original gloomy prognosis remained until after the operation. The adrenalectomy was the decisive factor in treatment; without it she would almost certainly have ended her days in a mental hospital.—I am, etc.,

London, W.1. E. A. BENNET.

Trendelenburg Tilt

SIR,—Few anaesthetists will disagree with the contention of Dr. J. M. Inglis and Mr. B. N. Brooke (*Journal*, August 11, p. 343) that modern anaesthetic technique can prevent that encroachment of the intestines upon the pelvic operating field which Trendelenburg's position was designed to diminish. Although their paper refers primarily to the *steep* tilt it nevertheless unfortunately implies that even a moderate (say 15°) tilt has no place in modern operating technique. During the synchronous combined excision of the rectum this degree of tilt is necessary if only to bring the perineum up to the level of the seated surgeon while leaving the table as a whole low enough for the standing operator to work comfortably in the abdomen. I feel sure my surgical colleagues at St. Mark's Hospital would be reluctant to abandon the "lithotomy-Trendelenburg" position for that operation.

From the anaesthetic viewpoint the authors' remarks upon the disadvantages of the position raise issues calling for further comment. The impression is given that it is regarded as a disadvantage to have to use controlled respiration and a cuffed tube. It is disturbing that, 10 years after the introduction of curare into anaesthetic practice, reference to a "partially curarized diaphragm" working against gravity should be additional evidence of a widely held, semi-mystical belief in the virtue of inadequate *spontaneous* respiration, as compared with efficient *controlled* respiration. One had hoped that the routine use of an apnoeic technique in major abdominal surgery (with its corollary of a cuffed tube) would no longer be discouraged by writers associated with a teaching hospital centre.

As far as the vasomotor system is concerned, if the patient is moved into a moderate degree of tilt by stages during the interval between induction and the approach to the pelvis and returned to the horizontal even more gradually during the corresponding period between peritoneal closure and the return to bed, the hydrodynamic disturbances of the circulation are minimal and cause little apprehension even in known "cardiac" cases. The speed at which the table is tilted appears to be more important than its final angle. Although it would be easier if the tubing of National Blood Transfusion Service giving sets were 18 in. (45 cm.) longer, it is still possible to have the transfused arm retained alongside the patient whether he is horizontal or tilted. The nerve palsy objection (which anyway only applies to a steep tilt) is then met by careful placing of the shoulder-rests.

In short, Sir, I feel it would be a pity if surgeons who asked for a moderate degree of Trendelenburg tilt were left with the impression that they were presenting their anaesthetist colleagues with a major problem involving an increased hazard for the patient.—I am, etc.,

Loughton, Essex. DONALD V. BATEMAN.

Antibodies Against Cancer

SIR,—Apropos your leading article (*Journal*, August 4, p. 290) on antibodies against cancer, would it be of interest to you to hear of the following experiment performed about 1940?

From an adenocarcinoma of the colon, removed at operation, about the size of a large cricket ball, non-tumour tissues were dissected away immediately as far as possible, and from the tumour masses an antigen was produced by the same method exactly as that used in the preparation in my laboratory of a Wassermann antigen, but using the malignant tissue in place of the human heart tissue. With this tumour-extracted antigen a Wassermann test was performed on about 25 of the sera which had been received that day for the ordinary Wassermann test, using the standard technique.

Two strong positives and one positive were found, and, on checking with the Wassermann bench, the results were identical with the Wassermann results: the remaining sera were negative by both tests.—I am, etc.,

Maidstone, Kent. E. R. JONES.

Shoe-fitting by X Rays

SIR,—While Dr. E. D. Dyson (*Journal*, August 4, p. 269) has clearly indicated the hazards from the *x*-ray fluoroscopes so commonly used in the shoe shops of to-day and has indicated the need for control measures to prevent harm from this source, may I suggest that the opportunity be taken by the Ministry of Health committee to consider the total prohibition of the use of these machines in the fitting of children's footwear?

There is no doubt that these machines have been found to be an excellent medium for salesmanship, and are used

mainly to impress parents with the need for the purchase of new footwear on the grounds of short-fitting shoes. The machine, of course, cannot give a proper estimate of the fit of a shoe, since it is only able to relate the length of the foot skeleton to the length of the sole of the shoe. It is quite impossible for a machine of this kind to estimate the width or girth required to give a true fitting of a child's foot, although cumbersome devices, which are rarely used, exist which claim to do this. This, of course, is the really important part of shoe-fitting, and can only be done by trained and experienced fitters. The introduction of an *x*-ray machine to a shop gives a sense of false security to the shop assistants and to the prospective purchasers regarding the fitting of the shoe and encourages the use of untrained and uninstructed girls straight from school to practise their salesmanship. This is done on the basis of a shoe's pleasing appearance to the eye and the extremely doubtful advantage of having looked at the foot skeleton under a "pedoscope."

The high incidence of foot deformity among school-leaving girls (almost certainly in the region of 75% showing hallux valgus caused by bad fitting of footwear) does call for some control in the shoe-fitting practice of the country. If no one were allowed to fit shoes to children and no shoes were allowed to be sold without the fitting being done by a trained and qualified fitter, then the need for the pedoscope would be obviated, hallux valgus would become a thing of the past, and the potential hazards from shop *x*-rays would be eliminated.

I hope the Ministry's committee will be able to use its influence to prohibit the use of these machines and to obtain the trade's co-operation to a system of shoe-fitting which would rest upon the trained eye and hand rather than the pseudo-scientific fitting that is accepted so glibly by the general public under pressure of the boot and shoe trade. The harm that is being done to children's feet and health is not nearly so much from the radiation of this toy as from the ignorance of the poorly paid shop assistants, who are so often dependent upon commission on sales to enable them to secure a reasonably adequate livelihood.

Dr. Dyson's article has given us an opportunity to review the whole position in relation to children's shoe-fitting, and, as one who has been interested in this subject for a number of years, I feel this opportunity should not be allowed to pass without making a real step toward the prevention of hallux valgus among the population as a whole.—I am, etc.,

London, W.5. W. G. BOOTH.

Medical Evidence at Inquests

SIR,—The letter (*Journal*, August 11, p. 356) of Dr. F. M. Rose, of Preston, as to coroners is of significant interest: I have no doubt that the present system is capable of improvement both locally, for some local authorities do not find it possible to see to all the needs of the coroner, and generally by alteration of the law. But the work has to be done by someone. Coroners as a whole are not averse to comment, even adverse comment, upon their methods, but it should be accurate. Dr. Rose clearly knows something about the subject-matter of his letter, but his allegation about a block grant is entirely untrue: his conclusion that the coroner personally benefits ("a direct saving to the coroner personally") appears to be almost libellous, though no person with any knowledge would take it seriously. How does he justify it, or does he retract?—I am, etc.,

London S.E.1. W. B. PURCHASE.

Chiropody Associations

SIR,—In your issue of August 4 (p. 308) you report an exchange of views between Mr. Somerville Hastings, M.P., and Mr. Robert Carr, M.P., the Parliamentary Secretary to the Minister of Labour, regarding the recognition of the Society of Chiropodists, during which Mr. Carr stated that "The British register was maintained by the B.M.A., which recognized only the Society."

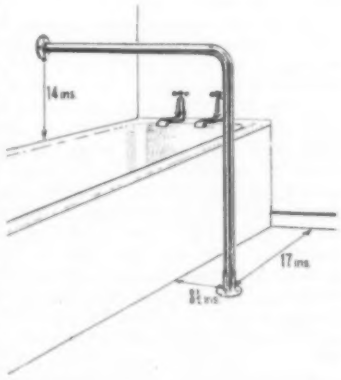
I think, for reasons of clarity, it should be pointed out that the "British register" (by which is meant the *National Register of Medical Auxiliary Services*, maintained and published by the Board of Registration of Medical Auxiliaries) is not maintained by the B.M.A., as such. The Board is an independent body set up in 1936 jointly by the B.M.A., the Society of Apothecaries of London, and a number of medical auxiliary organizations, to establish a register of properly qualified medical auxiliaries. The Society of Chiropodists is the only chiropody body recognized by the Board, because it is the only body whose standards of training, curriculum, and ethical rules are considered adequate.—I am, etc.,

London, W.C.1. A. M. A. MOORE,
President,
Board of Registration of Medical Auxiliaries.

Invalid Aid

SIR,—As a sufferer from Parkinson's disease, I find that one of its many disabilities is the difficulty of getting in and out of a bath. In hospitals it is hard work for one male nurse or two female nurses, and a frightening performance. At home I can do this practically unaided owing to a simple arrangement my wife devised some years ago to enable her to manage unassisted.

This device is a strong right-angled steel rod, fixed across and above the bath: one arm enters the wall through a socket 14 in. (35.5 cm.) above the rim of the bath, and 17 in. (43 cm.) from the taps; the other arm is firmly fixed into a 6-in. (15-cm.) socket screwed to the floor, leaving a clearance of 8½ in. (21.5 cm.) between it and the side of the bath to facilitate cleaning. Where the bath stands clear of the wall two vertical and one horizontal rods would be necessary and probably a central stay rod at right angles to the horizontal rod, fixed to the wall beyond the taps or right-angled to the floor.



Provided a person is able to use his arms it is very much easier to lower or pull himself up in the forward plane and especially in conditions where balance is affected. Most elderly, weak, or disabled people would find this arrangement a much greater help than side rails, and the use of it entails much less strain on the nursing staff with consequent time-saving, one nurse being able to manage with ease where two would normally be required.—I am, etc.,

Newcastle, Co. Down. F. S. MAYNE.

Effect of Glycyrrhetinic Acid on Eczema

SIR,—Recently glycyrrhetinic acid has been introduced in dermatology as having a similar action to hydrocortisone. We have tried to assess its value on a series of in-patients with various patterns of eczema, using the paired limb comparison technique, employing independent observers, and deciding the effect without knowing on which side the control ointment was applied. The preparations of glycyrrhetinic acid used were a 2% ointment supplied by Genatosan, and in the last six patients a 2% ointment marketed by Biorex Ltd. We first compared the effect with 1% hydrocortisone, and in eight patients the response to the hydrocortisone was greater. We next compared glycyrrhetinic acid ointment with ung. emulsificans aquosum (*B.P.*) and later with the

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exact inert base. In 12 out of 19 patients the side treated with the active ointment showed no difference from the control side. In three the active ointment was slightly better, and in four the inert base was slightly better. There did not appear to be any difference in the effect of the two makes of the glycyrrhetinic acid.

From this small series of cases it would seem probable that glycyrrhetinic acid in the two preparations used has no effect.—We are, etc.,

ROBERT P. WARIN.
CLIFFORD D. EVANS.

Bristol.

Sickling in African Community

SIR,—Drs. H. Lehmann and A. B. Raper are to be congratulated on the important contribution they have made to the problem of sickling in African communities (*Journal*, August 11, p. 333), but their article contains one misleading suggestion. It is not true that the loss of life from malaria acting differentially upon the normal homozygote can be reduced by the simple expedient of deferring malarial mortality until other diseases have reduced the child population. Their own figures show this to be an illusion. Thus in Table III they postulate 157 deaths of AA homozygotes from a mean population of ½ (648+491), or a mortality of 27%. Table IV shows 69 deaths from a mean population of ½ (282+213), again a mortality of over 27%. The reference to 6.9% of all children born alive is a red herring.

It is possible to carry the authors' conclusions a step further. Having considered the elimination of normal homozygotes both before and then after other mortality, they continue: "If malaria is imagined as causing deaths concurrently with other diseases . . . the figures observed would lie somewhere between the limits assigned." The "limits" referred to are in effect one and the same mortality of 27%, and it is easy to show that it remains the same even with concurrent mortality. Let us assume that the population is reduced by death so as to follow an exponential curve expressed by the equation $N.e^{-at}$, where N is the initial population and "a" the exponential rate of decline. Let "μ" be the uniform mortality affecting all children, and "m" the mortality due to malaria operating upon normal homozygotes only. The two population curves are then $P.e^{-\mu t}$ and $P.e^{-(m+\mu)t}$ respectively. The ratio of these populations at the onset is P/P or unity and after the lapse of time "t" becomes $\frac{P.e^{-(m+\mu)t}}{P.e^{-\mu t}}$ or e^{-mt}. In other words, the proportional reduction due to malaria is independent of other mortality operating and will be the same whether acting alone or concurrently.

The authors quote mortality rates from the Belgian Congo of 22 deaths from malaria per 1,000 per annum below the age of 3, and from Accra of 17 per 1,000 under 1 year and 10 per 1,000 from ages 1 to 5 years. These account for approximately 66 and 57 deaths per 1,000 exposed to infection and are still far from the required 27%. Support for the views that these rates are not far from the maximum likely to be found in susceptible populations can be given from data referring to Uganda itself. An analysis was made of all registered deaths of non-Africans in Uganda in the five-year periods straddling the years in which a census was taken. The death rates per 1,000 per annum from malaria in its widest meaning were:

	Death Rates per 1,000 per Annum			Cumulative Mortality to Age 15 per 1,000
	Under 1 Year	1–4 Years	5–14 Years	
1909–13	4	6	4	68
1919–23	4	1	2	29
1929–33	7	8	14	29
1946–50	2·9	3·6	6	12·5

These figures include deaths from "fever" and "cerebral malaria" as well as microscopically confirmed malaria, but on the other hand it is likely that deaths in the first months of life may be underestimated. The influence of modern methods of control is well illustrated, and it is interesting that the earliest rate approximates so well to that found among African children elsewhere.

From the available data there is still seen to be a big gap to be closed between the 24% reduction in population needed by this hypothesis and the 7% or so which malaria can effect. If sickling heterozygotes are not completely immune to malaria the gap would of course become larger.—I am, etc.,

Dundee. WILLIAM A. WILSON.

Prevention of Tetanus

SIR,—Your leading article (*Journal*, August 11, p. 348) emphasizes some of the difficulties inherent in the application of passive immunization against tetanus and renews the doubts which have recently arisen as to its overall prophylactic value. Few will now question the preference for active immunization; it is the practical difficulties which are the barrier retarding progress towards a complete civilian active immunization comparable with that pertaining in the Services.

The early fears that the use of the triple toxoid would necessarily result in the lowering of the antitoxin titres of any one of the three has now largely been dispelled by the recent work of Barr *et al.*[1] and Ungar.[2] But the more potent deterrent seems to be the question of the cost of mass triple toxoid immunization, and this bogy is frequently used as an argument against its introduction. It is a difficult one to refute, since it is not easy to ascertain what the present practice of passive immunization costs the nation. It can only be pointed out that in the three hospitals reviewed[3] the yearly cost of passive immunization alone must have been nearly £400, and that at least one large supplier of the diphtheria–tetanus–pertussis prophylactic makes no additional charge for the tetanus constituent of D.T.P.P. as against that for the diphtheria–pertussis prophylactic. One presumes that the Ministry of Health could, without difficulty, ascertain the saving of cost to the nation which active immunization might well afford apart from its intrinsic value, and could dispel the possible illusion that such an innovation would be as costly as is often suggested.

Finally, many recent authorities in America, Australia, and in this country have urged the necessity for a record card for inoculations and have deprecated haphazard and unrecorded immunizations. It has already been suggested that there seems to be no valid reason why the National Health Medical Card (form E.C.4) should not be redesigned to cover this need. Once again this suggestion has to overcome the inertia of the Ministry of Health before it can be implemented. The sooner a start is made in that quarter the sooner will civilian prophylaxis become as efficient as the excellent Barr–Sachs report[4] indicates that it has become in the armed Services.—I am, etc.,

London, N.W.1. N. H. MOYNIHAN.

REFERENCES

1 Barr, M., Glenny, A. T., and Butler, N. R., *British Medical Journal*, 1955, 2, 635.
2 Ungar, J., ibid., 1956, 1, 841.
3 Moynihan, N. H., ibid., 1956, 1, 260.
4 Barr, M., and Sachs, A., *Army Pathology Advisory Report*, 1955, W.O. Code No 11262.

Food-poisoning

SIR,—The main efforts to control food-poisoning in this country have been concentrated upon improving hygiene in kitchens and other places where food is prepared or sold. Despite the fact that this campaign has been waged for several years, the incidence of food-poisoning is still increasing. Sir William Savage (*Journal*, August 11, p. 317) is of the opinion that increased methods of exhortation will be necessary before this campaign has any great effect. Although this may be so, I believe, at least as far as salmonella infection is concerned, that it could be very

profitably aided by directing a little more attention at points earlier in the process of food production.

As an example of this, may I refer to the position with regard to emergency-slaughtered animals? For the benefit of your readers who are not acquainted with meat production I would mention that these are sick animals taken to abattoirs for slaughter in the hope that their carcasses will be suitable for human consumption. In large abattoirs a room is set aside for the slaughter of such animals, but in many small ones all animals, sick and healthy, have to be slaughtered out of necessity in the same room and by the same personnel. Meat inspection in these small abattoirs is usually not a continuous process, and consequently some considerable delay may occur before an emergency-slaughtered animal is officially inspected, during which time the slaughter of healthy animals continues.

Emergency-slaughtered animals have been responsible for some of the most severe outbreaks of food-poisoning ever recorded. It is not unusual, too, for some of them to be found to be suffering clinically from other diseases, such as tuberculosis, that are communicable to human beings. I firmly believe that emergency-slaughtering, particularly in the small abattoirs, merits much more serious attention from those concerned with the maintenance of public health.—I am, etc.,

Stock, Essex. H. WILLIAMS SMITH.

Broken Probe

SIR,—May I suggest that Dr. G. H. Gibbens (*Journal*, July 28, p. 240) buy one or two Jobson Horne's probes? These are standard equipment in E.N.T. work and will do all that his pieces of wire will do and will last longer than the owner. They are made of stainless steel and are about 18 cm. long and 2–3 mm. thick in the middle of the shaft, which is usually octagonal in cross-section and tapers towards the ends, one of which is flattened with fine lateral serrations on the terminal 1.5 cm. or so and the other of which carries a fine loop about 3 mm. in diameter.

The use of cut wire, as described by Dr. Gibbens, to do anything with an eye (or an ear) seems unwise. It is impossible to cut wire without leaving the ends rough. If the art of digital eversion of eyelids has not been acquired, a wooden "applicator" is the best instrument. The applicator undoubtedly is unsatisfactory, because of its excessive diameter, for mopping out ears. However, if any reader can suggest something more suitable for use at home by 'patients' relatives in those cases needing more frequent aural toilet than can be given by the practitioner, I shall be glad to hear of it.—I am, etc.,

Guillimh, Ireland. SEAGHAN UA CONCHUBHAIR.

POINTS FROM LETTERS

"Pop-gun" Containers

Dr. JOHN M. HARDY (Burnley, Lancs) writes: May I draw attention to a danger to children from the plastic containers of tablets with a well-fitting cork? When empty and with the stopper in position, a sudden squeeze projects the stopper with remarkable force—certainly equivalent to the old cork "pop-gun."

Innovation in Technique for Dental Gas

Dr. C. J. COOPER (Blanes, Spain) writes: ". . . A suitable mouth prop is inserted . . . and the child is instructed *to blow out and in through the nose*" (*Journal*, May 12, p. 1085—my italics). Dr. Arthur Tom appears to have thought of everything in his paper "An Innovation in Technique for Dental Gas," so I shall not cavil at the slight misuse of language in saying "blow . . . in" for "breathe in" when referring to the nose, if in practice he gets the more forcible respirations that he wants. But I should like to know why he does not simply say to his young patients, "Put your tongue on the roof of your mouth (or put your tongue up) and breathe hard in and out." Is it not possible that those whose "nasal respiration is not satisfactory" have simply omitted to put their tongues up in the moment of stress? The child has his mouth propped open and cannot ask questions, so is it not important to give very clear instructions?

Obituary

E. M. LOURIE, M.B., M.R.C.P., D.P.H.

Dr. E. M. Lourie, chief of the Section of Biological Standardization of the World Health Organization, died suddenly in Geneva on August 11 at the age of 52.

Born at Johannesburg, South Africa, on February 18, 1904, Emanuel Mannie Lourie obtained the London Conjoint diploma in 1927 and the London degrees of M.B., B.S. in 1928, after receiving his medical education at the University College Hospital Medical School. He took the D.T.M.&H. of the London School of Hygiene and Tropical Medicine in 1930, the D.P.H. in 1934, and was elected M.R.C.P. in 1948. Two years after qualification Lourie went to Palestine to work on leishmaniasis with his friend, Professor Saul Adler. In 1930 he joined the staff of the Liverpool School of Tropical Medicine, and in the following year became Rockefeller Research Fellow of the Medical Research Council and worked in Chicago with Professor W. H. Taliaferro. There he devised a method for testing drugs on avian malaria which subsequently was adopted in laboratories throughout the world. In 1934 he returned to Liverpool as a Beit Memorial Fellow under the direction of Professor Warrington Yorke, with whom he was intimately associated in continuous work on the chemotherapy of protozoal infections until the death of Professor Yorke in 1943. Lourie was then appointed the first director of the department of chemotherapy of the Liverpool School of Tropical Medicine and so served until 1948. After a short period in the department of pharmacology in Oxford he finally assumed the office of chief of the Section of Biological Standardization of the World Health Organization, a post which he held until his untimely death. In 1945 he was awarded the Chalmers Memorial Gold Medal by the Royal Society of Tropical Medicine and Hygiene for his outstanding contributions to tropical medicine.

A man of ability, indefatigable industry, and complete intellectual honesty, Lourie's publications were numerous and of high quality. The pharmacology of the synthetic drugs and the problem of drug-fastness were his special interest, and he did much to advance knowledge in each of these fields and published many papers on these and allied subjects. Together with Warrington Yorke he discovered the diamidine series of drugs and developed them in the treatment of protozoal infections of animals. When penicillin first became available it was Lourie who showed its efficacy against spirochaetal infections in laboratory animals and forecast its role in the treatment of human syphilis. This shortly afterwards was substantiated by himself and others. During the early years of the second world war he was in West Africa investigating an epidemic of sleeping sickness, and there he initiated extensive field trials on the treatment of the disease with the diamidine group of drugs, which fulfilled the promise of his initial experiments. On his return home the ship in which he and his wife were travelling was torpedoed.

As a man Lourie was charming and accomplished, and a delectable companion; no mean athlete, he equally was interested in the arts and muses. Of great personal integrity, he was singularly free from a desire for personal advancement and from those jealousies which may cloud scientific endeavour. His generosity to his junior colleagues is evident in the lists of authorship

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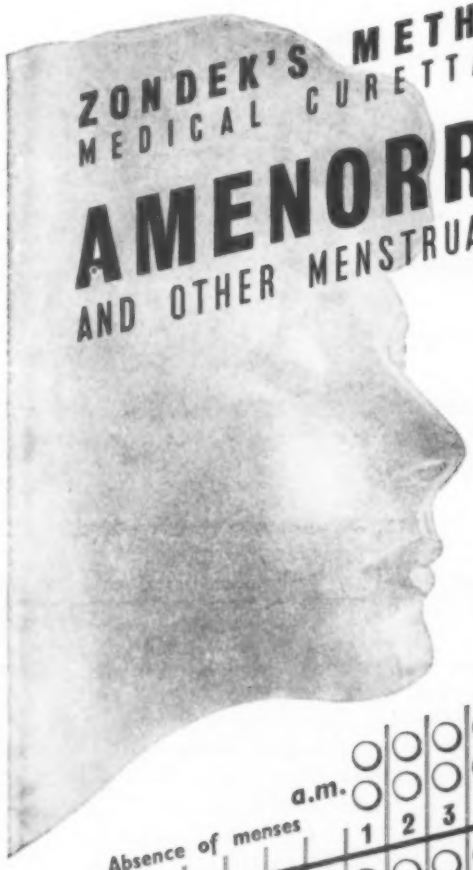

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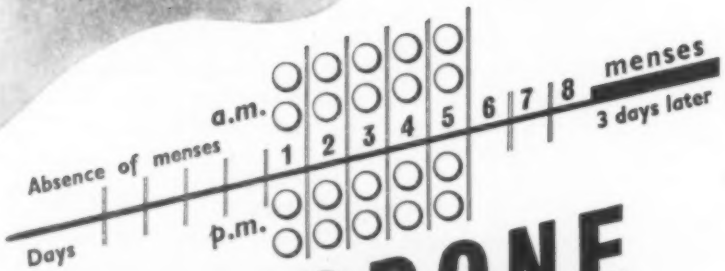

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of papers on which his name appears. They and his very numerous friends in various parts of the world share a great sense of loss with his wife, Olga, and their young son, Michael.—A. R. D. A.

LILIAN HUTTON, M.B., D.P.M.

The death of Dr. Lilian Hutton at the age of 52 on August 8 after a long illness has brought a sense of grief to her colleagues and patients, whom she so loved, at the Burden Neurological Institute, Bristol, at which she was clinical director.

Lilian Hutton was born on March 25, 1904, and was trained at the Royal Free Hospital, London, graduating M.B., B.S., London, in 1928. Her early experience in psychiatry was obtained at Harton Hospital, South Shields, and at Rainhill Hospital, Liverpool. In 1932 she took the D.P.M. of the English Royal Colleges, and in the following year obtained an appointment at Horton Hospital, Epsom. She left Epsom in 1939 to join the staff of the Burden Neurological Institute.

Dr. W. D. NICOL writes: In 1933 Lilian Hutton came south and I had the good fortune to have her as a colleague at Horton Hospital. She was the first medical officer to receive a clinical research appointment under the London County Council, and for some seven years she worked with me at the special malaria therapy centre, now the Mott Clinic, for the treatment of neurosyphilis. Her flair for research and her keen industry made for a happy team with Mr. Shute and myself, and several papers on the problems of neurosyphilis and malaria were published. It was a matter for regret at Horton when Dr. Hutton left to join Professor F. L. Golla as the clinical director of the Burden Neurological Institute. I always felt that there she was given a wider scope for her researches and I am sure the hopes which she entertained were abundantly fulfilled. At the Burden Institute her activities were switched to psychotherapeutic problems of the neuroses. Lilian Hutton was a remarkable person, and her death at the height of her powers is a severe loss to psychological medicine. To her mother, with whom she lived, we extend our sympathy.

Professor F. L. GOLLA writes: Dr. Hutton always desired to engage in psychotherapeutic research unhampered by the many difficulties and restrictions incidental to the organization of a large public hospital, and hence was willing on joining the Burden Neurological Institute to accept the material sacrifices involved in exchanging a Government position for the freedom of an autonomous research centre. Her earlier work at Horton in the establishment of the celebrated clinic for the malarial treatment of neurosyphilis, and her researches on the aetiology of schizophrenia at the Central Pathological Laboratory at Denmark Hill, made it possible for her to appreciate the nexus between bodily and mental disorder with full recognition of the validity of both psychological and physiological research methods.

At the Burden Neurological Institute in 1939, when she assisted at the introduction of electric convulsion therapy and leucotomy into this country, she published some pioneer papers on the psychological results of these methods and later participated in research work on imagery and neuroendocrinology. When war conditions made access to patients easier she was able to devote herself to research on the psychotherapy of neurotic conditions. Both as a clinician and as a laboratory worker she was very alive to the value of the contributions of physiological psychology, but she had the wisdom to realize that in the present state of our knowledge there is little to be gained, and much to lose, by any attempt to elucidate disorders of conduct by an exclusive use of either physiological or psychological methods. She considered a pragmatic approach as the one likely to be most fruitful. But, though she refused to be limited by methodological considerations, she came to see more and more clearly that phenomenalism is not enough when we apply our methods of description to psychiatry.

Of a deeply religious nature, she felt that no system of psychotherapy is likely to succeed if it does not attempt to deal with the patient's spiritual difficulties. Though she subscribed to the teaching of Jung, that a neurotic is essentially a person in search of his soul, she felt that Jung's concept could be more fully expressed by a more activistic attribution. To love, not to be loved, is, she maintained, the ultimate goal, in the quest for which psychological medicine requires the aid of religion. Love thus understood is not merely intrapersonal but must so be directed as to embrace the eternal values.

In her small clinic of in-patients and her larger collection of out-patients she obtained remarkable success with cases of neurotics of many years' standing. In some such cases that had hitherto proved to be refractory to every form of treatment her results were both dramatic and permanent. Though she wrote little her fame spread to other countries, and much of her time was given to answering inquiries from abroad and in interviewing colleagues from all parts of Britain. At the time of her death she was actively engaged in collating her great mass of clinical observations with a view to publication. She was loved by her patients and loved and admired by her colleagues. Those who knew her only as a physician mourn the loss in the fullness of her powers of a very great teacher and healer, and it is little short of a calamity that her early death has finally prevented her views from becoming made widely known.

H. P. PICKERILL, C.B.E., M.D., Ch.M., M.D.S. F.R.A.C.S.

Mr. H. P. Pickerill, consulting plastic surgeon to the Wellington Hospital, New Zealand, died on August 10 at the age of 77.

Henry Percy Pickerill was born in England, at Hereford, in 1879, and was educated at Hereford College. In 1896 he was articled to a dental surgeon in Hereford, where he worked until 1900, when he entered Birmingham University as a dental student. He had a brilliant career there, winning the Charles Greene Memorial Medal and the senior prize among other awards. He obtained the diploma of L.D.S. of the Royal College of Surgeons of England in 1903 and the Birmingham B.D.S. in the following year. Having decided to take a medical qualification, he graduated M.B., Ch.B. in 1905 while holding the appointment of demonstrator at the Birmingham Dental Hospital. In 1906 he became assistant surgeon at the hospital and lecturer on dental histology and pathology in the university. In 1911 he was awarded the Cartwright Prize and Medal by the Royal College of Surgeons of England for his essay on the prevention of dental caries, and in the same year he proceeded to the M.D. and the M.D.S.

Soon afterwards Pickerill went to New Zealand, where he held a teaching post at the University of Otago. But the first world war brought him back to England as a member of the 1st New Zealand Expeditionary Force. Eventually he attained the rank of lieutenant-colonel in the New Zealand Medical Corps and became officer in command of the New Zealand section at Queen Mary's Hospital for facial injuries at Sidcup, in Kent. By this time he was widely known for his skill as a plastic surgeon, and for his services he was appointed O.B.E. in the 1919 Birthday Honours. He was promoted C.B.E. in the New Year Honours of 1923 for valuable services rendered since the war in connexion

with facial and jaw operations on wounded soldiers in New Zealand. In the same year he proceeded to the Ch.M. After the war Pickerill returned to his work in New Zealand, being appointed surgeon in charge of the facial and jaw department at the Dunedin General Hospital and director of the dental school of the University of Otago. In 1927 he moved to Australia and settled in practice in Sydney, becoming honorary plastic surgeon to the Royal North Shore Hospital there. He did not stay long in Australia, however, but went back to New Zealand in 1935, this time to Wellington, where he was plastic surgeon to the Wellington Hospital and, later, to the Middlemore Hospital, Auckland. He was elected a Fellow of the Royal Australasian College of Surgeons in 1930. In later years he and his wife, who is also a plastic surgeon, did much valuable work at the Bassam Hospital, Lower Hutt, correcting congenital deformities in children.

A member of the British Medical Association for nearly fifty years, Pickerill was chairman of the Otago Division in 1922. He was also a foundation member of the British Association of Plastic Surgeons; a former vice-president of the Section of Odontology of the Royal Society of Medicine; and an honorary member of the Société Belge de Stomatologie. An expert on facial surgery, he contributed numerous papers on his special subject to the literature. He was twice married: first, in 1906, to Miss Mabel Knott, and secondly, in 1934, to Miss Cecily M. Clarkson, a medical graduate of the University of New Zealand. He had three sons and two daughters.

Dr. L. D. B. COGAN died at his home at Northampton on August 6 at the age of 81. Lee Danby Buxton Cogan was born on January 23, 1875, the son of Dr. L. F. Cogan, who was medical officer of health for the county borough of Northampton for twenty-six years and a justice of the peace there. From Epsom College he went on to Guy's Hospital, qualifying L.S.A. in 1898. He saw service as a medical officer with the Ashanti Field Force and in the Northern Territories of the Gold Coast before qualifying for the diploma of L.R.C.S.Ed. in 1903. A little later he settled in general practice at Northampton in partnership with his father. Always keen on the Volunteer movement, Dr. Cogan joined the Territorial Army as a lieutenant in the R.A.M.C. some years before the outbreak of the first world war in 1914, during which he was present at the Gallipoli landings. Later he held the post of assistant director of medical services of the 29th and Southern Divisions, and was in command of the 88th Field Ambulance with the acting rank of lieutenant-colonel when he was awarded the D.S.O. in the 1919 New Year Honours. He was also mentioned in dispatches. After the war he returned to his practice at Northampton, and for a time acted as senior clinical assistant at the Metropolitan Ear, Nose, and Throat Hospital when the hospital was in Fitzroy Square, London. In 1925 he obtained the diploma of L.M.S.S.A. For many years he was medical officer to the Northampton Post Office and factory surgeon for the Northampton district. He was also medical officer to the prison. In 1935 he was president of the Medical Practitioners' Union and had served on the council of the Union. From 1938 until he resigned in 1953 Dr. Cogan was a member of the Northampton County Borough Council, being appointed an alderman in 1952. He leaves a widow, one son, and three daughters.

With the death of Dr. H. C. BARTLETT on June 16 Saffron Walden has lost one of her oldest and most distinguished citizens. He was 92 years of age. Born in London on July 7, 1863, Hedley Coward Bartlett began his medical career at the age of 16 as an apprentice to Dr. Henry Stear, a general practitioner in the market town of Saffron Walden, in Essex. After qualifying M.R.C.S., L.R.C.P. from the Middlesex Hospital in 1886, he held a number of house appointments at the Middlesex Hospital and also became clinical assistant at the Royal London Ophthalmic Hospital. Later he returned to Saffron Walden as a general practitioner, having bought Dr. Stear's practice on the latter's retirement. He practised there for over fifty years and was on the staff at the Saffron Walden General Hospital for over forty-three years as surgeon (1890–1933) and later as senior surgeon. During the first world war he was locally responsible for two Red Cross hospitals for convalescent soldiers and also for the wounded at the Saffron Walden General Hospital. He practised midwifery in remote cottages and farmhouses, often assisted only by a "handy woman" and a coachman holding a lamp. Dr. Bartlett practised in an age when the tradition of the family doctor played a vital part in the lives of the community. He was friend and confidant, and many to-day still pay tribute to his kindliness and brilliance as a surgeon and his devotion to medicine and healing. In the early days Dr. Bartlett covered many miles on his rounds in carriage and pair or in a dog-cart. He was an early pioneer of motoring and one of the first doctors in East Anglia to possess a motor-car. Interested in the legal aspect of medicine, he was called to the Bar at Gray's Inn. He was a member of the Medico-Legal Society and medical referee for many insurance companies. He was a Fellow of the Society of Antiquaries, being particularly interested in old furniture, of which he made a large collection. In 1912 he bought and restored a small mediaeval castle, known as Pembridge Castle, on the Welsh border, where he lived after he retired in 1939. In 1891 he married Miss Flora Sibley, daughter of Dr. Septimus Sibley, a London general practitioner. She died in 1948. He is survived by one son and four daughters. His eldest daughter on qualifying went into partnership with her father, the son joining the partnership ten years later.

The obituary of Dr. D. F. WHITAKER was printed in the *Journal* of August 11 (p. 365). C. M. S. writes: May a further tribute to Donald Whitaker be paid by one privileged to claim friendship with him, particularly on central committees during the past five years? No one could fail to be impressed by his deep sincerity, which added great weight to his invariably sound opinion. Ever jealous of the honour and traditions of his beloved profession, he had, like so many of his generation, become increasingly perturbed at many of the effects and implications of the N.H.S. that have become increasingly apparent since 1948: but nevertheless he firmly continued to give of his best, with far too great a strain on his constitution. Few committees could ever have had a more conscientious and valuable member, and yet, with it all, he managed to enjoy the good things of life to the full, as evidenced at the Brighton Meeting. He was impatient with the second-rate, and his acuity of vision enabled him to detect the sham when covered by a mask of plausibility.

W. E. S. writes: May I, as a fellow student of Donald Whitaker at University College Hospital, add a few words to the obituary notice published in the *Journal*? As a student he was a keen member of the hospital rugger team and an active supporter of numerous student functions. He was a tall man of distinguished appearance, but spoke always in a quiet voice, giving an outward impression of imperturbability. His dealings with patients were marked by conscientiousness, kindness, and common sense. Although in later years he became a member of many committees, his sense of humour prevented him from becoming pontifical. He was brought up in Hendon, where he retained many contacts and will be much missed, as also at the annual gatherings of old U.C.H. students. He married a daughter of the well-known surgeon, the late Mr. Mower White, and had three children, one of whom is entering the medical profession. To them and his widow deep sympathy is extended in their bereavement.

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Brit. Med. J., 1956, *ii* 200.

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Miss Pat Hornsby-Smith, Parliamentary Secretary, Ministry of Health, has stated why the Ministry could not take advantage of the offer a number of people had made to give in their lifetime one of their eyes to help save the sight of other people who would otherwise be completely blind. Replying to Lieutenant-Colonel Marcus Lipton, Labour M.P. for Brixton, who asked for an official ruling from the Ministry, Miss Hornsby-Smith says in a letter dated August 13 that similar offers have been made from time to time direct to the department. "The law on the matter is not certain, but I am advised that it is at least possible that for a surgeon deliberately to remove a sound eye from a living person, even with that person's consent, might be held to be a criminal offence. In any case it seems most unlikely that surgeons would be willing to perform the operation. At the same time I am glad to be able to let you know that we have recently been able to improve the arrangements for supplying the hospitals which carry out corneal grafting with eyes derived from patients who have died in hospitals, and we hope that the shortage from which these hospitals have been suffering is being brought to an end. None of this, of course, detracts in any way from the splendid spirit of the people who have offered to give their eyes while they are still alive."

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

In Congregation on August 4 the following degrees were conferred:

M.D.—J. M. S. Knott, I. H. Mills, K. Brown-Grant, R. H. B. Protheroe, J. P. D. Thomas, M. F. Bethell, M. T. Parker.

M.B., B.CHIR.—*A. H. H. Johnson, *R. W. Lister, B. M. King, V. Whitehead, [1]I. A. D. Todd, F. Mansfield, *P. S. Bentlif, *P. D. Jackson, J. Shaw, *W. R. B. Jones, *G. Maisel.

M.B.—*L. G. Whitby, N. F. Jones, R. E. Scott, *G. M. Petrie, *G. Yates, *C. P. K. Watson, *R. T. Barnie-Adshead, *A. L. Gunn, T. W. Young, R. W. M. Smith, *O. W. Hill, *R. K. L. Percival Smith, J. K. Ll. Jones, G. E. G. Williams, *C. A. Fox, G. W. M. Faris, N. D. Kilpatrick, M. G. Smedley, P. C. Bewes, T. W. Hoskins, *P. F. Gray, A. C. Brown, *Jennifer M. D. Gibson, *Elizabeth D. Hocking, *Frances J. Keegan, *Brenda J. Sheail, *Jean E. Vallis, *Margaret F. Beard, Eleanor M. Bray, *F. G. Cooper, *V. Cope, *K. A. McL. C.-O. Swinburne.

*By proxy.

UNIVERSITY OF GLASGOW

The following degrees were conferred on July 7:

M.D.—[1]R. J. Calvert, [2]R. C. Curran, [1]J. T. G. Ewan, [1]K. C. Wybar.

CH.M.—[2]W. T. Irvine, [2]W. B. Stirling.

M.B., CH.B.—R. T. Abbott, A. Abdurahman, G. Abrami, D. C. Agbo, Eleanor McL. Aitken, J. M. Allan, W. K. G. Allan, Catherine F. Anderson, R. L. Andrew, Sarah L. Armour (Mrs. Hemming), A. A. Atkinson, S. Azimuddin, Moira C. Baird, W. L. M. Baird, W. H. Beattie, J. M. Bell, Margaret J. A. Blackwood, T. Blair, B. B. Borthwick, M. F. Brewster, [1]K. A. C. Brown, [1]N. MacL. Brown, J. S. Bryden, G. D. Burnett, A. T. Calder, J. A. Caldwell, Veronica R. Carson, Georgina M. Chadwin, I. A. Chisholm, G. A. Clark, C. Comyns (name changed from Comens), Ruth S. R. Conacher, P. Connelly, F. M. Cranna, J. M. Crombie, Martha K. Cuthbertson, J. Dalling, T. W. B. Davidson, W. C. Davidson, Jean S. Dick, G. Drummond, A. A. Efunkoya, W. M. Elder, I. L. Felstein, A. K. Foli, W. Frank, A. S. Fraser, J. B. W. Galloway, [1]D. G. Garvie, I. Ilan J. Geddes, S. W. George, I. B. Gibson, Jane M. B. Gilchrist, Mary L. Girkins, J. F. Glencross, J. G. Graham, R. C. Graham, J. H. Greig, R. C. Grieve, W. D. Guy, Elizabeth H. Hamilton, A. J. Hardie, G. A. Hayes, Robina M. Herd, Helen E. Holms, R. W. Irvine, Elizabeth J. Ives, [1]L. Johnman, D. Johnston, Julia A. Keane, J. Keatings, J. Kelly, [1]I. R. Kernohan, I. F. Kerr, J. F. Kirk, I. B. Kirkland, A. H. Kleinglass, J. A. Laithwaite, T. W. Lindsay, Elizabeth R. Lohoar, I. T. Loudon, C. J. Macaulay, Sheila H. McCulloch, A. R. McCutcheon, C. McDonald, W. W. McDougall, Grace N. Macfarlane, W. G. McGhee, R. D. Macgill, J. G. McHugh, J. MacKay, J. D. McKean, B. R. Mackenna, Harriet B. MacKinnon (formerly Shaw), Sheila A. H. McLaren, J. Maclean, B. G. P. Macnamara, N. McNeil, A. D. M'Neill, R. L. McRitchie, J. A. McShane, A. J. Marshall, W. Marsnall, A. MacO. Michael, W. Miller, G. McN. Milne, R. G. McK. Mitchell, D. L. Morrison, J. Morrison, J. J. Morrow, N. Morton, A. Munro, D. S. Munro, R. K. Murray, A. Neilson, Barbara J. Newman, T. L. O'Donnell, B. Patel, E. H. Paterson, M. L. Peacock, J. L. Price, A. J. Rintoul, K. K. T. Robertson, Ann F. M. Savage, I. W. H. Scott, Joanna E. M. Scott, Mary B. Simpson, M. W. Smellie, I. Soutar, D. Stephen, R. McK. Still, J. Stothers, F. W. C. Surgenor, W. Susskind, R. M. R. Taylor, A. B. M. Telfer, [1]J. A. Thomson, R. G. B. Turner, D. A. L. Watt, Doris S. Whiteford, S. Wotherspoon, D. G. Young, J. J. Young.

[1]With commendation. [2]With honours.

UNIVERSITY OF EDINBURGH

At a graduation ceremonial on July 18 the following degrees and diplomas were conferred:

M.D.—B. A. Bembridge, [2]W. P. Cockshott, [1]J. R. Fountain, [2]I. C. Lewis.

CH.M.—R. B. Duthie (awarded gold medal for thesis).

PH.D.—*In the Faculty of Medicine*: K. B. Singh, M.S. (*In absentia*), H. P. Sinha, M.B., B.S. (*In absentia*), Maung Mya Tu, M.B., B.S.

M.B., CH.B.—E. I. Adam, Margaret Aitken, W. B. Aitken, Mary M. Anderson, O. A. Audain, P. M. Barnes, J. S. Barr, J. C. J. Ll. Bath, R. W. Bell, F. E. P. Bernard, G. W. Beveridge, R. D. R. Birtwhistle, L. McM. Black, Joan M. Bradley, D. P. Braid, C. Brough, Rose M. Brown, Bridget M. Buchanan, D. A. Buchanan, G. O. D. Busby, A. Cameron, A. E. Cameron, J. A. Cameron, R. V.-V. Cavaroli, W. G. Charlesworth, G. J. A. Clunie, A. D. Colledge, S. J. Cooper, I. C. Crawford, C. Croll, G. G. K. Davidson, C. A. R. Dennis, Ruth Douglas, [2]T. W. Fenton, A. J. W. Fordyce, D. F. Foster, G. L. Frank, Christina A. Fulton, P. W. Gasson, W. K. Gibb, A. A. M. Gibson, A. B. J. Gilbert, W. L. A. Gilchrist, J. Gordon, J. G. Govan, D. E. Graham, G. S. Graham, G. C. Greig, A. R. Grieve, J. Gunn, M. J. Hall, T. Hamilton, Agnes M. Hay, C. P. Hellon, M. A. Henderson, W. E. Howieson, J. J. Huston, D. C. Ingham, J. T. Ireland, P. Jacques, Ann R. Karnitschnig (formerly Gaddum), G. M. Kay, K. M. G. Keddie, I. W. Kemp, R. Lampard, [2]A. O. Langlands, Annabel M. Lauchlin, [2]D. Leak, P. Lee, J. R. B. Livingstone, E. B. Longton, J. N. McCormick, H. R. Macdonald, Isabella S. Macdonald, F. M. McGurk, Catherine J. McHardy, J. C. MacInnes, I. MacG. MacIntyre, J. C. McIntyre, B. Mackay, I. M. Mackay, D. S. Mackenzie, J. Mackie, Shirley A. Mackintosh, Gillian E. Mackrell, A. R. MacLeod, J. Macleod, J. P. A. McManus, F. J. McMinn, J. MacSween, D. O. Marsh, J. McK. Mason, M. D. Middleton, D. R. Millar, E. N. C. Milne, Norah Milne (formerly Symington), W. M. U. Moffat, D. Morton, N. J. Moule, Aileen C. Munro, J. C. M. Murphy, W. D. Murray, E. K. Newman, Marjorie S. Newton, F. T. Nicoll, D. L. Norrie, N. D. Ogilvie, F. R. Orr, Elspeth M. Paterson, R. S. Phillips, K. Protheroe, A. G. C. Renwick, G. R. Rogers, R. M. Savage, J. M. Scott, D. S. Sibbald, B. Simpson, Catherine M. Simpson, Barbara Somerville, N. A. McC. Somerville, D. A. Spencer, S. C. E. Spink, B. R. Stead, J. D. Sutherland, Norma E. I. Temple, W. J. Thomson, M. A. Turner, B. I. Tyson, J. A. Waddell, Brenda Wainwright, A. A. Walker, Aline M. Watson, S. I. Williams, A. R. Wilson, P. Wilson, W. L. Yule.

DIPLOMA IN PUBLIC HEALTH.—A. H. Duncan, W. M. Fee, R. Y. Forbes, Ruth E. Graham-Yooll, J. M. H. Hopper, R. A. Ingles, Elinor K. Johnston, Ko Ko, H. R. W. Miller, A. R. Mills, S. R. Nair, Kee Saik Ooi, R. S. H. Pasqual, D. Shearer, R. Steele, W. Williams.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—G. C. Anbunathan, A. Annamalai, G. I. Forbes, Tun Tun Hlaing, A. D. McIntyre, M. P. Misra, P. Rabindran, A. McQ. Robertson, J. R. K. Robson, A. W. H. Thomson, Dorothy N. Ullah, S. K. Vaish, J. Wilkinson, V. Zaman, O. K. Hazari.

The following scholarships, etc., were awarded in the Faculty of Medicine: *Cameron Prize in Practical Therapeutics*, jointly to Professor W. D. M. Paton and Dr. Eleanor Zaimis in recognition of their work on methonium compounds. *Ettles Scholarship and Leslie Gold Medal in Medicine, James Scott Scholarship in Obstetrics and Gynaecology, Beaney Prize in Anatomy and Surgery*, A. O. Langlands. *Scottish Association for Medical Education of Women Prize* and *Dorothy Gilfillan Memorial Prize*, Margaret Aitken. *Buchanan Scholarship in Obstetrics and Gynaecology, Mouat Scholarship in the Practice of Physic, Keith Memorial Prize in Systematic Surgery*, and *Murdoch Brown Medal in Clinical Medicine*, David Leak. *Annandale Gold Medal in Clinical Surgery*, D. P. Braid. *Royal Victoria Hospital Tuberculosis Trust Gold Medal*, G. O. D. Busby. *Graduate Research Fellowships*, G. D. Campbell, A. Peters, J. H. Tait, Elizabeth M. Humphreys. *Sir David Wilkie Research Fellowship in Medicine*, R. B. Cross. *James Traquair Scholarship*, J. Hindley. *Graduate Research Scholarships*, E. W. Horton, Margaret A. J. Moffat, J. A. Hodgson. *Graduate Travelling Scholarships*, J. A. L. Clark and T. T. S. Ingram. *Ellis Prize in Physiology*, E. A. Harris. *Gunning Victoria Jubilee Prize in Public Health and Social Medicine*, J. A. H. Lee. *William Leslie Prize in Medicine*, L. J. P. Duncan and B. C. Paton (equal). *Lawrence Poole Prize in Rehabilitation after Poliomyelitis*, W. J. W. Sharrard. *Greig Medal for Tropical Medicine*, J. Wilkinson. *Wellcome Prize and Medal in the History of Medicine*, E. W. Horton.

[1]Highly commended for thesis. [2]Commended for thesis. [3]With honours.

The Services

Major-General D Bluett, O.B.E., late R.A.M.C., Deputy Director of Medical Services, Eastern Command, has been appointed Honorary Physician to the Queen, in succession to Major-General A. Sachs, C.B., C.B.E., retired.

Colonel W. D. Hughes, C.B.E., late R.A.M.C., has been appointed Honorary Physician to the Queen, in succession to Colonel (Honorary Brigadier) J. T. Robinson, O.B.E., retired.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 4** (No. 31) and corresponding week 1955.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1956					1955				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	3	0	7	5	0	5	0	1
Dysentery	603	94	120	3	3	392	63	141	19	5
Encephalitis, acute	3	1		0		3	0		0	
Enteric fever:										
Typhoid	1	0	0	0	1	24	2	5	1	
Paratyphoid	8	0	1 (B)	0		5	1	0	0	1
Food-poisoning	334	23		3		361	44		9	
Infective enteritis or diarrhoea under 2 years				5	36				15	40
Measles*	3,220	258	39	48	168	9,971	130	33	59	78
Meningococcal infection	26	4	4	0	1	11	0	9	0	
Ophthalmia neonatorum	30	0	8	0		26	0	2	0	
Pneumonia†	196	11	81	1		188	13	66	6	
Poliomyelitis, acute:										
Paralytic	73	4	8	0	23	146	22	18	0	1
Non-paralytic	58	2				161	36			
Puerperal fever§	220	27	5	2		253	34	8	3	
Scarlet fever	426	25	41	8	9	196	11	24	21	8
Tuberculosis:										
Respiratory	620	61	99	17		512	61	112	14	
Non-respiratory	87	6	15	5		71	3	29	2	
Whooping-cough	2,146	191	215	22	56	1,553	83	79	91	81

DEATHS in Great Towns	1956					1955				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	1	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	1	0	1	0	1	6	0	1	0	3
Influenza	6	0	1	0	0	1	0	0	0	0
Measles		0	0	0	0		0	0	0	1
Meningococcal infection		0	0				0	0		
Pneumonia	148	26	9	6	4	114	12	8	3	2
Poliomyelitis, acute	1	0			0	4	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	50	2	6	0	1	55	9	3	0	3
Non-respiratory		0	2	0	0		2	3	0	1
Whooping-cough	1		0	0	0	0	0	0	1	1
Deaths 0–1 year	194	29	21	7	7	175	19	13	4	14
Deaths (excluding stillbirths)	4,321	627	477	98	118	4,057	549	453	77	154
LIVE BIRTHS	8,196	1117	896	222	409	7,052	1075	883	237	366
STILLBIRTHS	191	26	16			180	17	18		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications in the week ending August 11 (32nd week of the year) were as follows: paralytic 54 (73), non-paralytic 75 (58), total 133 (131). This is an increase of 2 compared with the previous week, the figures for which are in parentheses.

Cases notified from the beginning of the year (with rate per 100,000 in parentheses) are as follows for districts of relatively high incidence: Macclesfield M.B. 25 (69), Whitehaven M.B. 22 (87), Ennerdale R.D. 18 (63), Yeovil M.B. 19 (79), Guildford M.B. 33 (70), Manchester C.B. 241 (35), Woking U.D. 21 (38), Reigate M.B. 17 (35), Middleton M.B. 14 (33), Guildford R.D. 15 (32).

Week Ending August 11

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 275, whooping-cough 2,134, diphtheria 4, measles 2,685, acute pneumonia 136, acute poliomyelitis 133, dysentery 443, paratyphoid fever 12, and typhoid fever 5.

Infectious Diseases

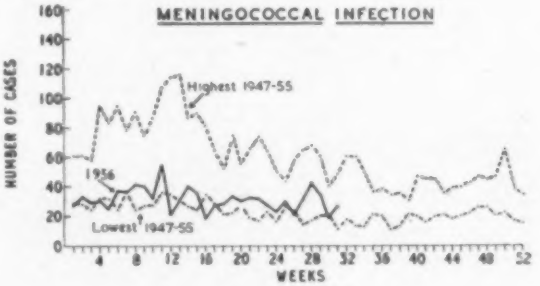
The incidence of infectious diseases fell in England and Wales during the week ending August 4. The decreases in the number of notifications were 242 for whooping-cough, from 2,388 to 2,146; 240 for dysentery, from 843 to 603; 147 for scarlet fever, from 573 to 426; 85 for food-poisoning, from 419 to 334; 50 for measles, from 3,270 to 3,220; and 29 for acute poliomyelitis, from 160 to 131.

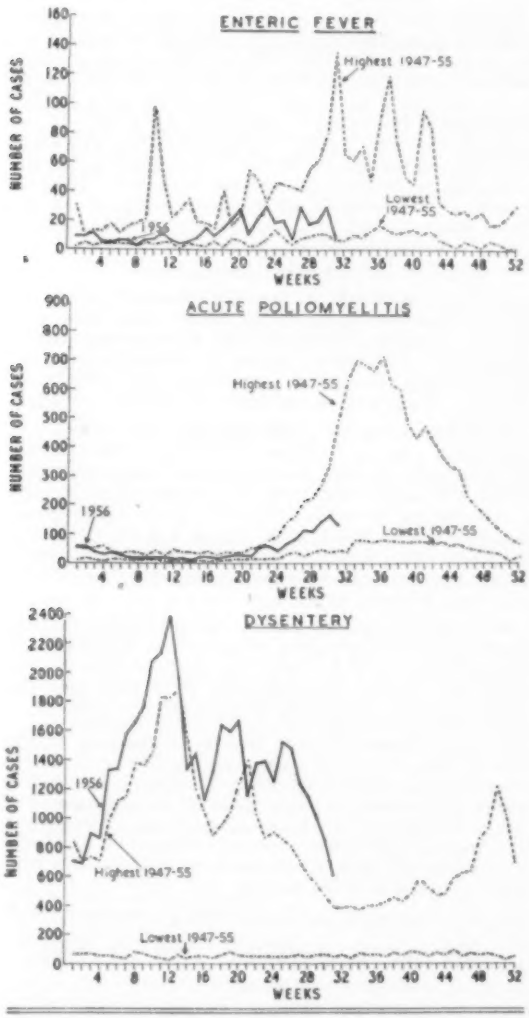
The largest declines in the notifications of whooping-cough were 86 in Yorkshire West Riding, from 236 to 150, and 40 in Warwickshire, from 201 to 161. A fall in the incidence of scarlet fever occurred throughout the country, but no large local fluctuations were recorded. The largest variations in the local trends of measles were decreases of 105 notifications in London, from 363 to 258; 75 in Cornwall, from 284 to 209, and a rise of 99 in Oxfordshire, from 96 to 195. The outbreak in Oxfordshire was mainly confined to two areas, Witney U.D. (102) and Witney R.D. (54). No case of diphtheria was notified. This is the first week since records have been kept that a case of diphtheria has not been reported.

The chief centres of dysentery were Yorkshire West Riding 106 (Rotherham C.B. 39, Leeds C.B. 22); London 94 (Hackney 10, Greenwich 9, Stepney 9); Lancashire 69 (Liverpool C.B. 17); Warwickshire 59 (Coventry C.B. 38, Birmingham C.B. 15); Leicestershire 26 (Leicester C.B. 24).

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1947–55 are shown thus ------, the figures for 1956 thus ———. Except for the curves showing notifications in 1956, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Medical News

New Medical School in Africa.—The University College of Rhodesia and Nyasaland has appointed a committee to advise it on the desirability and practicability of establishing a medical school. The committee is to prepare proposals for the training curriculum, research facilities, buildings, equipment, and staffing, and estimates of the costs. The following are the members: Mr. L. FARRER-BROWN (Director, the Nuffield Foundation), chairman; Professor W. MELVILLE ARNOTT (William Withering Professor of Medicine, University of Birmingham); Professor T. H. DAVEY (Middlemass Hunt Professor of Tropical Hygiene, University of Liverpool); Professor A. D. M. GREENFIELD (Dunville Professor of Physiology, Queen's University of Belfast); Professor P. B. MEDAWAR, F.R.S. (Jodrell Professor of Zoology, University College, London); Professor R. MILNES WALKER (Professor of Surgery, University of Bristol); Dr. HONOR M. V. SMITH (May Reader in Medicine, University of Oxford). The committee will make a preliminary visit to the Federation of Rhodesia and Nyasaland in January, 1957.

"Tranquillizers."—In a statement published in the *Pharmaceutical Journal* of August 11 (p. 97) the council of the Pharmaceutical Society calls attention to "the recent introduction of a number of new products which owe their use to their depressant action on the central nervous system." The statement goes on: "While these drugs are not advertised to the public a widespread public knowledge of them has been created by newspaper articles, and there is a substantial demand for them otherwise than on prescription. The indiscriminate use of such drugs is, in the council's opinion, against the public interest, and the council are approaching the Ministry of Health requesting an early consideration of this class of drugs. Pharmacists are advised not to display them or to supply them unless satisfied they will be taken on medical advice."

High Energy Radiation Unit.—A new high energy radiation treatment unit at Cookridge Hospital, Leeds, was opened recently by the Princess Royal. This unit marks the completion of the first stage in the development of Cookridge Hospital as a regional radiotherapy centre, a development made possible by the co-operation of the Board of Governors of the United Leeds Hospitals, the Rockefeller Foundation, the British Empire Cancer Campaign (Yorkshire Council), the University of Leeds, and the Leeds Regional Hospital Board. The new unit is claimed to be unique in Great Britain in that it has been specially designed for the dual purpose of radiotherapy and radiation research. There is only one other therapeutic source of radio-cobalt of equivalent size in the country, a Canadian gift to the British Empire Cancer Campaign. Smaller cobalt units exist, however, in various British centres, the two in the Leeds region being at the General Infirmary at Leeds and the Radium Institute at Bradford. The Cookridge Unit has been established to provide new facilities for the treatment of cancer and for the study of the physical, chemical, and therapeutic action of high energy radiation. This sharing of a powerful radiation source by radiotherapists, chemists, and physicists was planned because of its economic use of expensive apparatus and also to bring together a group of medical and non-medical men working on problems which have much in common and are fundamental to radiobiology. The source of high energy radiation at this new unit will emit radiation equivalent to a machine working at about 3,000,000 volts.

Hunter House Memorial Fund.—A committee representing the University of Glasgow, the Royal Faculty of Physicians and Surgeons of Glasgow, and the East Kilbride Development Corporation has been set up to raise a fund for the renovation and preservation of the birthplace of William and John Hunter at Long Calderwood, East Kilbride (illustrated below). A nucleus of nearly £3,000 has been raised in Scotland. A total sum of £20,000 is aimed at, and, of this, £3,500 will be needed urgently to restore the fabric of the house, leaving the balance as an endowment fund. It is planned to organize a board of trustees with appropriate representative interests to maintain the restored house as a memorial, a museum, a place of pilgrimage, and, possibly, as a research centre. In its appeal, which is now

[Harry Blake, Strathaven

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A blank space denotes disease not notifiable or no return available.

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	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	3	0	7	5	0	5	0	1
Dysentery	603	94	120	3	3	392	63	141	19	5
Encephalitis, acute	3	1		0		3	0		0	
Enteric fever:										
Typhoid	1	0	0	0	1	24	2	5	1	
Paratyphoid	8	0	1 (B)	0		5	1	0	0	1
Food-poisoning	334	23		3		361	44		9	
Infective enteritis or diarrhoea under 2 years				5	36				15	40
Measles*	3,220	258	39	48	168	9,971	130	33	59	78
Meningococcal infection	26	4	4	0	1	11	0	9	0	
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Tuberculosis:										
Respiratory	620	61	99	17		512	61	112	14	
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Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	1	0	1	0	1	6	0	1	0	3
Influenza	6	0	1	0	0	1	0	0	0	0
Measles		0	0	0	0		0	0	0	1
Meningococcal infection		0	0				0	0		
Pneumonia	148	26	9	6	4	114	12	8	3	2
Poliomyelitis, acute	1	0			0	4	0			0
Scarlet fever		0	0	0	0		0	0	0	0
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Infectious Diseases

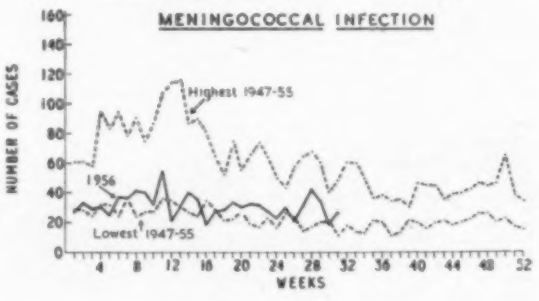
The incidence of infectious diseases fell in England and Wales during the week ending August 4. The decreases in the number of notifications were 242 for whooping-cough, from 2,388 to 2,146; 240 for dysentery, from 843 to 603; 147 for scarlet fever, from 573 to 426; 85 for food-poisoning, from 419 to 334; 50 for measles, from 3,270 to 3,220; and 29 for acute poliomyelitis, from 160 to 131.

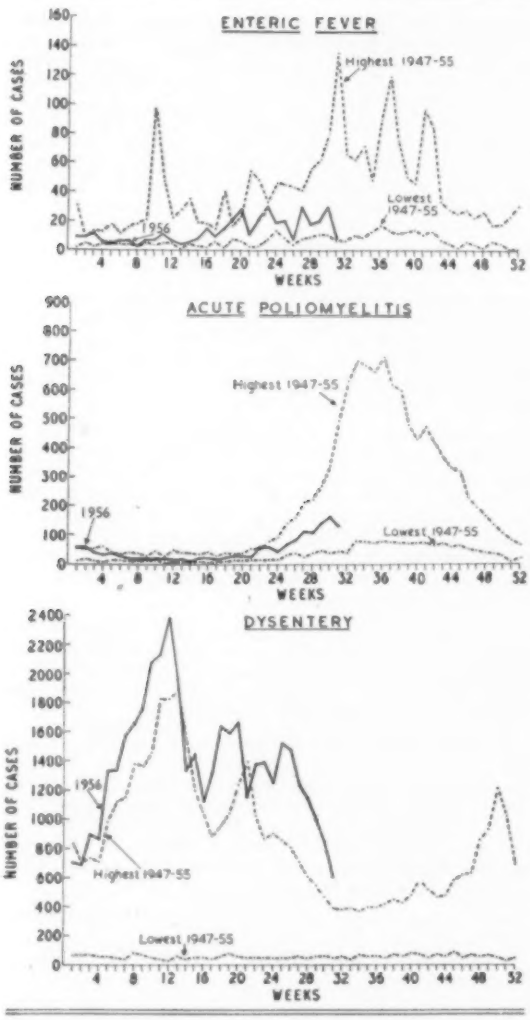
The largest declines in the notifications of whooping-cough were 86 in Yorkshire West Riding, from 236 to 150, and 40 in Warwickshire, from 201 to 161. A fall in the incidence of scarlet fever occurred throughout the country, but no large local fluctuations were recorded. The largest variations in the local trends of measles were decreases of 105 notifications in London, from 363 to 258; 75 in Cornwall, from 284 to 209, and a rise of 99 in Oxfordshire, from 96 to 195. The outbreak in Oxfordshire was mainly confined to two areas, Witney U.D. (102) and Witney R.D. (54). No case of diphtheria was notified. This is the first week since records have been kept that a case of diphtheria has not been reported.

The chief centres of dysentery were Yorkshire West Riding 106 (Rotherham C.B. 39, Leeds C.B. 22); London 94 (Hackney 10, Greenwich 9, Stepney 9); Lancashire 69 (Liverpool C.B. 17); Warwickshire 59 (Coventry C.B. 38, Birmingham C.B. 15); Leicestershire 26 (Leicester C.B. 24).

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1947–55 are shown thus ------, the figures for 1956 thus ———. Except for the curves showing notifications in 1956, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Medical News

New Medical School in Africa.—The University College of Rhodesia and Nyasaland has appointed a committee to advise it on the desirability and practicability of establishing a medical school. The committee is to prepare proposals for the training curriculum, research facilities, buildings, equipment, and staffing, and estimates of the costs. The following are the members: Mr. L. FARRER-BROWN (Director, the Nuffield Foundation), chairman; Professor W. MELVILLE ARNOTT (William Withering Professor of Medicine, University of Birmingham); Professor T. H. DAVEY (Middlemass Hunt Professor of Tropical Hygiene, University of Liverpool); Professor A. D. M. GREENFIELD (Dunville Professor of Physiology, Queen's University of Belfast); Professor P. B. MEDAWAR, F.R.S. (Jodrell Professor of Zoology, University College, London); Professor R. MILNES WALKER (Professor of Surgery, University of Bristol); Dr. HONOR M. V. SMITH (May Reader in Medicine, University of Oxford). The committee will make a preliminary visit to the Federation of Rhodesia and Nyasaland in January, 1957.

"Tranquillizers."—In a statement published in the *Pharmaceutical Journal* of August 11 (p. 97) the council of the Pharmaceutical Society calls attention to "the recent introduction of a number of new products which owe their use to their depressant action on the central nervous system." The statement goes on: "While these drugs are not advertised to the public a widespread public knowledge of them has been created by newspaper articles, and there is a substantial demand for them otherwise than on prescription. The indiscriminate use of such drugs is, in the council's opinion, against the public interest, and the council are approaching the Ministry of Health requesting an early consideration of this class of drugs. Pharmacists are advised not to display them or to supply them unless satisfied they will be taken on medical advice."

High Energy Radiation Unit.—A new high energy radiation treatment unit at Cookridge Hospital, Leeds, was opened recently by the Princess Royal. This unit marks the completion of the first stage in the development of Cookridge Hospital as a regional radiotherapy centre, a development made possible by the co-operation of the Board of Governors of the United Leeds Hospitals, the Rockefeller Foundation, the British Empire Cancer Campaign (Yorkshire Council), the University of Leeds, and the Leeds Regional Hospital Board. The new unit is claimed to be unique in Great Britain in that it has been specially designed for the dual purpose of radiotherapy and radiation research. There is only one other therapeutic source of radio-cobalt of equivalent size in the country, a Canadian gift to the British Empire Cancer Campaign. Smaller cobalt units exist, however, in various British centres, the two in the Leeds region being at the General Infirmary at Leeds and the Radium Institute at Bradford. The Cookridge Unit has been established to provide new facilities for the treatment of cancer and for the study of the physical, chemical, and therapeutic action of high energy radiation. This sharing of a powerful radiation source by radiotherapists, chemists, and physicists was planned because of its economic use of expensive apparatus and also to bring together a group of medical and non-medical men working on problems which have much in common and are fundamental to radiobiology. The source of high energy radiation at this new unit will emit radiation equivalent to a machine working at about 3,000,000 volts.

Hunter House Memorial Fund.—A committee representing the University of Glasgow, the Royal Faculty of Physicians and Surgeons of Glasgow, and the East Kilbride Development Corporation has been set up to raise a fund for the renovation and preservation of the birthplace of William and John Hunter at Long Calderwood, East Kilbride (illustrated below). A nucleus of nearly £3,000 has been raised in Scotland. A total sum of £20,000 is aimed at, and, of this, £3,500 will be needed urgently to restore the fabric of the house, leaving the balance as an endowment fund. It is planned to organize a board of trustees with appropriate representative interests to maintain the restored house as a memorial, a museum, a place of pilgrimage, and, possibly, as a research centre. In its appeal, which is now

(Harry Blake, Strathaven

extended to all medical men, the committee states that "urgent action is necessary to save this national historic monument as a fitting memorial to the two brothers whose names will ever be gratefully remembered for their unique achievements in the advancement of medical knowledge." Cheques should be made payable to the "Hunter House Memorial Fund" and sent to the Hon. Treasurer, Royal Faculty of Physicians and Surgeons, 242, St. Vincent Street, Glasgow, C.2.

Mental Health Research Fund Awards.—A grant of £200 has been made to Dr. JAMES A. HISLOP, of the department of human ecology and university health service, Cambridge, for investigation of the length of stay of patients admitted to Fulbourn Hospital from the Isle of Ely during the past hundred years. This area has been chosen because of its "immobile" population, which for generations has been served by the same hospitals. A Leverhulme grant has been made to the University of Leeds towards the cost of a senior research fellowship awarded to Dr. MAX HAMILTON, senior lecturer in the department of psychiatry, who is investigating constitutional and other aspects of the patient suffering from paranoid disorders with a view to finding some tests or assessments which will give information about the probable response to treatment by electric convulsion therapy or insulin shock. A travelling fellowship has been awarded to Dr. R. P. HULLIN, lecturer in the department of biochemistry, University of Leeds, to enable him to spend a year chiefly in the department of physiological chemistry, University of Pennsylvania, investigating new biochemical methods which may be applied to the study of the blood in manic-depressive psychoses and endogenous depression.

Forensic Clinic in Toronto.—A Forensic Clinic has been opened recently in Toronto by the Department of Health of Ontario. While under the jurisdiction of the Department of Health, the Clinic also forms a division of the Toronto Psychiatric Hospital, and as such is affiliated with the University of Toronto. It carries out psychiatric appraisals on cases referred by the courts of Metropolitan Toronto, and in suitable cases psychotherapy is given. On such cases, and on those referred by probation officers, a specialized function of the clinic will be research on the problem of the sex offender. Cases of sex deviation are being received from a wider field than the courts—for instance, from private doctors and community services, etc. At present there is one full-time psychiatrist and one full-time psychologist on the staff. A social worker will be appointed in the immediate future, and a full-time research worker will be added within a matter of months. Further additions to the staff are expected in due course.

Retirement of Medical Librarian.—Mrs. EILEEN R. CUNNINGHAM, librarian of the school of medicine of Vanderbilt University, Nashville, Tennessee, has retired after 31 years of service. Since 1939 she had been professor of medical library science at Vanderbilt. In 1948 she was president of the Medical Library Association and received the first Marcia C. Noyes award for outstanding achievement in medical librarianship. Mrs. Cunningham has served on numerous international and national committees concerned with library services and with the documentation and interchange of scientific literature, and she has been active in promoting the recently organized International Association of Medical Libraries. The best-known of her written works is *Classification for Medical Literature*, the fourth edition of which we reviewed earlier this year (March 3, p. 499). Miss ELEANOR G. STEINKE, assistant librarian at Vanderbilt since 1946, will succeed Mrs. Cunningham.

COMING EVENTS

Doctor and Law.—The seventh International Congress of Catholic Doctors takes place in Scheveningen, Holland, during September 9–15. The subject is "The Doctor and the Law." Particulars from the Secretariate, 35, Herenstraat, Utrecht, up to September 1, and thereafter from the Palace Hotel, Scheveningen.

Lectures for Parents of Deaf Children.—The Deaf Children's Society has arranged a course of six lectures to help parents of deaf children. These will take place at the National Institute for the Deaf, 105, Gower Street, London, W.C.1, and will be as follows: September 13, 7 p.m., "The Deaf Child in the Family"; September 27, 7 p.m., "Lip-reading"; October 4, 7 p.m., "Auditory Training"; October 16, 7 p.m., "Language for Juniors"; November 1, 7 p.m., "Language for Seniors"; November 15, 7 p.m., "Reading Readiness." The lectures will be given by experts and the charge will be 1s. 6d. per lecture or 5s. for the complete course. Further particulars from WILLA A. MOOJEN, 92, New Cavendish Street, London, W.1.

Anthropology and Psychiatry.—Dr. MARGARET MEAD, of the American Museum of Natural History, New York, will talk on "The Contribution of Social Anthropology to Psychiatry" in the lecture theatre at Maudsley Hospital, Denmark Hill, London, S.E.5, on Friday, September 14, at 12 noon. Postgraduates are invited to attend.

Mackenzie Industrial Health Lecture.—The B.M.A., in conjunction with the Association of Industrial Medical Officers, announces that the sixth Mackenzie Industrial Health lecture will be given by Dr. R. S. F. SCHILLING on September 25 at 3 p.m. in the Great Hall, B.M.A. House, Tavistock Square, London, W.C.1. His subject will be "Assessing the Health of the Industrial Worker." All, lay and medical, interested in industrial medicine are invited. There will be no charge for admission.

Nutrition in Pregnancy.—The Scottish Group of the Nutrition Society is holding a symposium in Dundee on Saturday, September 29, on human and animal nutrition in pregnancy. Further particulars from Dr. J. DAVIDSON, The Rowett Institute, Bucksburn, Aberdeenshire.

London County Medical Society.—A meeting of the Society will be held at 5.30 p.m. on October 4 at the County Hall, Westminster Bridge, London, S.E.1. The society will be addressed by Sir CLEMENT PRICE THOMAS, and his subject will be "Carcinoma of the Lung." Members of the Association of Industrial Medical Officers, the Middlesex County Medical Society, and members of the London Divisions of the B.M.A. are invited.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Clift.—On August 8, 1956, to Dorothy (formerly Newell), M.B., Ch.B., wife of Arthur Clift, F.R.C.S., a daughter—Cecilia Margaret—a fifth child.

Eton.—On August 10, 1956, to Ilse (formerly Ursell), wife of Bruce Eton, M.B., M.R.C.O.G., of 1, High Street, Trumpington, Cambridge, a daughter—Rachel Caroline.

Heyworth.—On August 11, 1956, at Bank Hall Maternity Hospital, Burnley, to Freda and Frederick Heyworth, a daughter.

Levy.—On August 16, 1956, to Dr. and Mrs. Basil Levy, of 63, Anfield Road, Liverpool, a son.

MARRIAGES

Bhattacharyya—Bagchi.—On February 3, 1956, at Calcutta, Bhabani Bhattacharyya, F.R.C.S., to Puraby Bagchi, M.A.

DEATHS

Armstrong.—On August 5, 1956, at 514, Anniesland Road, Glasgow, William Hunter Stirling Armstrong, M.B., Ch.B., aged 79.

Baird.—On August 7, 1956, at 44, Station Road, Blackpool, James Campbell Baird, M.B., Ch.B.

Bradley.—On August 7, 1956, at Fremantle, Overwallop, Hants, Neville Bradley, M.B., Ch.B.

Brough.—On August 8, 1956, at 30, Craigleith Hill Gardens, Edinburgh, David Sands Brough, M.C., M.B., Ch.B., D.P.H.

Christie.—On August 3, 1956, Arthur William Stark Christie, M.B., Ch.B., F.R.C.S.Ed., of 4, Glencairn Crescent, Edinburgh.

Cogan.—On August 6, 1956, at Highfield House, Northampton, Lee Danby Buxton Cogan, D.S.O., L.R.C.S.Ed., aged 81.

Garnett.—On August 9, 1956, Graham Hogg Garnett, M.D., of 14, Croom's Hill, Greenwich, S.E.

Goldie.—On August 3, 1956, Ellis Gordon Goldie, M.D., of 11, Park Avenue, Mansfield, Notts, aged 79.

Gow.—On August 8, 1956, at Nestlea, Newbury, Berks, Henderson Gow, M.B., Ch.B.

O'Driscoll.—On August 3, 1956, at Lydney and District Hospital, Lydney, Gloucestershire, John Patrick O'Driscoll, M.B., B.Ch., of Bream, Gloucestershire.

Slocombe.—On August 2, 1956, Bernard Atkinson Slocombe, M.B., Ch.B., of Springfield, Keighley, Yorks.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Life Expectancy of Doctors

Q.—*What is the life expectancy of medical practitioners as compared with the general population? Please give figures for various countries, if such are available.*

A.—In the middle of the last century Neison[1] examined the mortality experience of members of the Royal Medical and Chirurgical Society, and found 96 deaths at ages 26–70 compared with 97.1 in the corresponding general population.

Hill[2] studied the early records of the Royal College of Physicians, and for various periods has compared the expectation of life of physicians, at age 35, with that of peers, with the following result :

	R.C.P.	Peers
1570–1689	30.3 years	28.6 years
1690–1749	32.1 ,,	31.0 ,,
1750–99	35.3 ,,	33.7 ,,

On the basis of the Registrar-General's occupational mortality data for 1910–12 for England and Wales, Hill calculated the expectation of life of medical practitioners aged 35 to be 32.7 years, compared with 31.7 years for all males. In 1921–3 and 1930–2 the Registrar-General[3] found the standardized mortality of male medical practitioners aged 20–65 to be respectively 1% and 6% higher than that of the general population. No later official figures for England and Wales have been published.

In Scotland, in a 25-year follow-up study of 899 Glasgow medical graduates of 1923–6, Meiklejohn[4] found their mortality "a good deal lighter than the mortality of the Scottish population as a whole." In France in 1907–8,[5] death rates per 10,000 population in the total population and among physicians and pharmacists were as follows:

	Age in Years			
	25–	35–	45–	55–64
Total population	80	112	178	320
Physicians and pharmacists ..	70	111	194	442

In the United States of America, Dublin and Lotka[6] reported the expectation of life of physicians aged 30 in 1925 to be 38.01 years, compared with 37.60 for the general population. In 1938–42 Dublin and Spiegelman[7] found that "physicians experienced practically the same longevity and mortality as white males of the same ages in the general population." Expectations of life at age 25 were:

	Male	Female
Physicians	43.54	47.10
U.S. white population	43.31	46.86

Diseases with high mortality rate amongst physicians were leukaemia, gall-bladder disease, cerebral haemorrhage, heart disease, arteriosclerosis, and cirrhosis of liver. Their mortality was low from syphilis, tuberculosis, prostatic disease, non-automobile accidents, and ulcer of the stomach and duodenum. The mortality of specialists[8] was only 71% of that of non-specialists.

In an occupational mortality survey[9] covering ten States of the United States in 1930, the mortality of physicians and surgeons was 87% of that of all occupied males in selected occupations.

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1. Neison, F. G. P., *J. statist. Soc.*, 1852, **15**, 193.
2. Hill, A. B., *British Medical Journal*, 1925, **1**, 754.
3. Registrar-General, *Decennial Supplement, England and Wales, 1931*, Part IIa, Occupational Mortality, 1938, p. 137. H.M.S.O.
4. Meiklejohn, A., *British Medical Journal*, 1953, **1**, 930.
5. Huber, M., *Bull. Statist. gen. France*, fasc. IV, 402, 1912. (Quoted by Daric, J. (1951). *Vital Statistics Special Reports*, Vol. 33, No. 10, U.S. Publ. Hlth Serv.)
6. Dublin, L. I., and Lotka, A. J., *Length of Life*, 1936, p. 226. Ronald Press Co., New York.
7. —— and Spiegelman, M., *J. Amer. med. Ass.*, 1947, **134**, 1211.
8. —— —— Ibid., 1948, **137**, 1519.
9. Whitney, J. S., *Death Rates by Occupation Based on Data of the U.S. Census Bureau, 1930*. New York, National Tuberculosis Association, 1934. Quoted by Daric (see ref. 5).

Radiography as a Career after Unilateral Oophorectomy

Q.—*Should a girl who has had a cystic ovary removed be discouraged, on genetic grounds, from her intention of becoming a radiographer? The remaining ovary was normal at operation.*

A.—There is no reason, from a genetic point of view, why this girl should be discouraged from taking up radiography as a career. The fact that one ovary has been removed is not relevant in assessing any genetic hazard from the effects of irradiation. The genetic effects of ionizing radiation depend on the fact that an increased rate of mutation of genes, in the chromosomes of the germinal cells, occurs as the result of accumulation of dose. The possibility of some genetic effects is not influenced by the fact of whether both ovaries are present or whether one has been removed—that is, whether the normal complement or half that complement of germinal cells are present—and there is no greater danger in the case of this girl.

The conditions of employment of radiographers are governed by the recommendations of the International Commission on Radiological Protection, recommendations which have recently been reinforced by the report of the Medical Research Council Committee on radiation hazards.[1] The relevant recommendation is that an individual occupationally exposed—for example, a radiographer—"should not be allowed to accumulate more than 50 r of radiation to the gonads, in addition to that received from the natural background, from conception to the age of 30 years." An accumulated dose of 50 r is an estimate of the dose which would produce a doubling of gene mutation rate. Paragraph 188 of the Medical Research Council report states : "One may conclude that, if a relatively small group of prospective parents receives a doubling dose of radiation, no noticeable effects will be produced either on their immediate offspring or upon their descendants. For levels of radiation up to the doubling dose, and even some way beyond, the genetic effects of radiation are only appreciable when reckoned over the population as a whole and need cause no alarm to the individual on his own account.

REFERENCE

1. Medical Research Council, *The Hazards to Man of Nuclear and Allied Radiations*. 1956, Cmd. 9780. H.M.S.O., London.

Inhalation of Mucolytic Agents

Q.—*What is the value of inhalation therapy with the modern mucolytic agents?*

A.—These mucolytic agents are claimed to reduce the viscosity of sputum, thereby making it easier to expectorate. To understand how they might act, it is necessary to describe how viscid secretions form in the bronchi. Respiratory mucus is a gel of fibrous protein and polysaccharide molecules, held together by linkages which normally include water molecules. The more water the gel contains the longer these linkages become, making the network looser and weaker. Therefore the viscidity of the mucus varies inversely with its water content.

Sometimes, as in fibrocystic disease and after the use of atropine-like drugs, mucus is secreted in a viscid dehydrated state. Under normal circumstances it is the drying of the mucus after secretion which renders it viscid and difficult to expectorate. During quiet breathing air reaches the main bronchi saturated with water at body temperature, having been humidified in the upper respiratory passages. If this is prevented, as it is by tracheotomy or endotracheal anaesthesia or during hyperventilation, then air will take up moisture from the bronchial mucus, leaving it increasingly viscid. Air saturated at body temperature contains three times as much water as air saturated at room temperature, but an aerosol at room temperature contains less than twice as much. Partially dried viscid mucus in the bronchi will imbibe water from a saturated atmosphere and become less viscid, and it will imbibe a little water from air partially saturated by forming an aerosol at room temperature Thus

a simple aerosol of water may reduce the viscidity of mucus. Mucus dried to the point of crusting will not imbibe moisture unless first broken down by chemical action.

Two kinds of "mucolytic" solutions for administration as aerosols have been used. The first contains a detergent, glycerin, and sodium bicarbonate. There is no evidence that such a solution affects the viscidity of mucus *in vitro*, and no controlled trials of its effect in man have ever been published. The only theoretical advantage of the solution over water is that it forms a more stable aerosol which may carry more water into the bronchi. The second type of solution contains trypsin, which is claimed to be specifically mucolytic. Trypsin is, in fact, a proteolytic enzyme which will damage the mucosa if used in sufficient concentration to affect dried mucus. Even premalignant changes in bronchial mucosa have been reported after the use of purified trypsin.[1] Lastly, trypsin is a foreign protein and its repeated use leads to sensitization.

No safe specific mucolytic agent has yet been discovered. In its absence prevention of viscid secretions is better than treatment. This is best done by ensuring an adequate fluid intake, eschewing atropine-like drugs, and by increasing the water saturation of inspired air.

REFERENCE

[1] Farber, S. M., Pharr, S. L., Traut, H. F., Wood, D. A., and Gorman, R. D., *Lab. Invest.*, 1954, 3, 33.

Athlete's Foot in a School

Q.—*What is the best method of dealing with an outbreak of athlete's foot in a secondary boys' school? Should the use of shower baths be prohibited in school?*

A.—Shower-bath floors favour the epidemic spread of fungous infection of feet. The regular scrubbing of such floors with fungicidal detergents and the wearing of slippers reduces the risk. Regular washing of feet, the wearing of cotton socks which are regularly boiled, and the use of dusting powder for the toes and feet are also important prophylactic measures.

It is important first to find the causative fungus by culture, for some are curable and others incurable. Infection by *Trichophyton rubrum*, which is becoming more common in this country, is very difficult to eradicate.

Benzoic and salicylic acid ointment or lotion (3% of each) at night and a fungicidal powder (undecylenic acid types) by day are a good method of treatment. There are, however, many other effective fungicides, including the mercurials and dyes. Brilliant green (½%) and perchloride of mercury (½%) in spirit is also effective, but stains clothes. The presence or absence of infection in the nails is important, and, if present, it may be necessary temporarily to remove the nails. Disinfection of socks and shoes by formalinization is also wise.

Involution of the Uterus and Oestrogens

Q.—*Does the exhibition of oestrogens during the puerperium, to suppress lactation, delay involution of the uterus?*

A.—No.

Inheritance of Friedreich's Ataxia

Q.—*How is Friedreich's ataxia inherited? A woman, whose twin brother died from the condition at the age of 23, wishes to marry. What is the prognosis regarding her life and the chance of her children being affected?*

A.—The clinical conditions labelled Friedreich's ataxia are not homogeneous. The great majority of those with early onset behave as if due to one or more recessive genes, and the illness is usually uniform within families and independent of sex. Much more rarely, dominant genes may give a somewhat similar clinical picture, these types showing much more variation of expression within families. While, therefore, it is probable that the gene concerned in the present patient's family is recessive and that there is little chance that she will develop the condition or will have affected children (assuming she does not marry a near relation), a careful family history should be taken and an expert neurological examination made of the patient herself and of her parents for minimal signs of the disease.

NOTES AND COMMENTS

Functional Ciliary Spasm.—Dr. THOMSON HENDERSON (Hursley, Hants) writes: May I comment on your expert's explanation on functional ciliary spasm ("Any Questions?" July 28, p. 254), which, while orthodox in conception, is, when analysed, incapable of realization? According to established convention the vascular choroid functions as a counterweight to the lens and the unstriated ciliary muscle is actuated by a single nerve. If these two tissues were able to function in such a manner they would be absolutely unique in the whole range of the animal kingdom. Nowhere can a vascular structure be found subjected to constant stress or unstriated muscle actuated except by two nerves and functioning accordingly. The physiological function of unstriped muscle is to contract into a phase of rest, such as is appreciated by every human being on emptying the bladder. Thus it is that the contracted unstriped fibres support the zonular curvature and maintain the lens flattened. As discussed in my book *Principles of Ophthalmology* (p. 132), asthenia from whatever cause results in diminution of the general tonus of the body. The neuromuscular mechanism, that maintains the body erect, sags, the individual stoops, and the atonic stomach dilates. Similarly, the atonic ciliary muscle is unable to support the lens traction and likewise sags. The zonular curvature is lowered and lenticular myopic refraction induced. This sequence of events is the very opposite of the so-called spasm, and its treatment is essentially constitutional.

OUR EXPERT replies: Although the precise action of the ciliary muscle has been debated for many years it is now widely accepted that the action of both portions of the ciliary muscle is to slacken the suspensory ligament of the lens, causing the lens to become more convex. Furthermore, the circular fibres act directly as a sphincter which diminishes the circumference of the ring formed by the ciliary body and hence also aids in relaxing the suspensory ligament of the lens. It is interesting to compare the unstriped muscle of the urinary bladder with that of the ciliary body, but surely the neuromuscular mechanism of a hollow viscus such as the bladder is a very different matter. Whatever objection may be raised to the orthodox explanation of the action of the ciliary muscle, it still remains a fact, which can be proved by mere observation, that in functional ciliary spasm of any appreciable degree there is an accompanying spasm of the medial recti. If the process causing the "over accommodation" were atonic in nature then one would hardly expect an accompanying contraction of the synergic medial recti muscles.

Prolonged Constipation in Children.—Mr. E. W. GODDING (Westminster Laboratories, Ltd., London, N.W.1) writes: As manufacturers of the "senokot" standardized senna preparations discussed by Mr. H. Reid and your expert ("Any Questions?" August 11, p. 374), may we comment on the question of costs? Your expert is correct in saying that two drams (7 ml.) of liquid paraffin daily and a tablet of senokot daily is about one penny a week, in either case, but for prolonged constipation the comparison may be very different. While liquid paraffin has to be given indefinitely, senokot dosage is required at less frequent intervals, and usually dosage can be gradually reduced and eventually discontinued.

Correction.—In the Epidemiological Table in the *Journal* of August 18 (p. 426) the number of deaths in the first year of life in the 17 principal towns of Scotland should have been shown as 21, and the deaths at all ages (excluding stillbirths) as 482; these numbers were inadvertently transposed.

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SUPPLEMENT TO THE

BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 25 1956

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TAX ASSESSMENT OF PART-TIME CONSULTANTS

CROWN APPEAL

The Crown has appealed against the decision of the Special Commissioners of Income Tax on the assessment of the remuneration of five part-time consultants (*Supplement*, August 18, p. 103), and the appeal will be heard in due course by a judge of the High Court.

SUPPLEMENTARY OPHTHALMIC SERVICES

FLAT LENSES

The following is the text of a letter (E.C.L. 49/56) from the Ministry of Health to clerks of executive councils.

I am directed by the Minister of Health to refer to the provision of the Statement of Fees and Charges that flat lenses are to be supplied for reading glasses unless curved lenses are prescribed as necessary, or are supplied at the applicant's request on an additional payment by him.

The Minister has been informed that a large part of the present manufacture of flat lenses will cease in the near future, and he is considering whether this will involve provision in the Statement of Fees and Charges for the supply of curved lenses for reading glasses without limitation. In view of existing stocks of flat lenses, which are less expensive than curved ones, he does not, however, propose to alter the present provisions immediately on the cessation of production, and I am to emphasize that the requirements about supply of flat lenses with reading glasses should be observed unless and until they are modified. It is most undesirable, for the sake both of fairness between patients and of use of existing stocks of lenses, that any tendency should develop among prescribers of prescribing as a matter of course curved lenses for reading glasses as "necessary." If, therefore, the Ophthalmic Services Committee have reason to think that such a tendency is developing either generally or on the part of individuals, they will no doubt approach the persons concerned and explain, in so far as the change in procedure appears to be connected with an expectation that flat lenses will go out of use, that a change of practice on such grounds is not in accordance with a reasonable interpretation of the prescriber's current responsibilities under the Statement of Fees and Charges and is unfair to other prescribers and their patients, and that the Committee are informed that stocks of flat lenses are ample for the time being.

Should there be any signs of a general tendency to prescribe curved lenses as necessary for reading glasses, the Ophthalmic Services Committee should consider sending a circular letter to prescribers explaining the position and, where opticians are concerned, of enlisting the help of the local optical committee.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Keeping Up With the Times

SIR,—Frederick Scott Oliver is a safe man to quote, and *The Times* is to be congratulated upon going to this source for the conclusion of their leading article on Suez. You, Sir, are to be congratulated and thanked for repeating it (*Journal*, August 18, p. 406).

I wonder if your readers are familiar with another quotation from F. S. Oliver, which at the present time seems more appropriate to our own professional troubles. It runs as follows: "When lawyers monopolize political power—even when they merely preponderate, as of late years they have seemed to do more and more in all democratic countries, whether of the monarchical or republican type—they invariably destroy by insensible gradations that which is most worth preserving in man or State, the soul. Their method is to strangle slowly like ivy."—I am, etc.,

Selby, Yorks. JOHN C. GILLIES.

Remuneration Claim

SIR,—Unlike some of my colleagues who have written to the *Journal* recently regarding remuneration, I am neither surprised nor dismayed by the rejection of our claim. I am not surprised, because the Government is at long last supposed to be trying to do something positive to halt inflation; extra-special appeals for restraint are being made, and, though these will be ignored by trade union leaders, it would be impolitic to grant an increase in remuneration to doctors with all the publicity that this will entail. In this regard the B.M.A. is much to blame. It held back, with its mistaken policy of restraint, when claims were being made by other professions, and being granted.

Neither am I dismayed by the Minister's rejection. What I expected from a politician, and what would have dismayed me, would have been the embarkation upon prolonged negotiations which would have gained for us some derisory increase in 1960 or maybe 1961. Now at least we know where we stand. I expected some sort of declaration and lead from the B.M.A. before this time. Is the B.M.A. waiting for our indignation to subside? Are we going to plead with the Minister that we should at least be allowed to start negotiations? If we do start negotiations there must be a definite foreseeable date by which time they shall be

complete, and there must be no equivocation about the amount of the claim. If negotiations are not completed by a certain date the arrangements must have been made by that date for a mass resignation. The public will suffer, but that is one of the reasons why pay claims are settled quickly.

I am reminded of a pay claim by nurses in a mental hospital in, I think, Brisbane. Negotiations dragged on for two years, until one day the nurses did not turn up for work. The Minister of Health visited the hospital and agreement was reached in two days. There is a moral in that somewhere.—I am, etc.,

London, W.1 A. W. BEARD.

SIR,—I am in full agreement with the proposals put forward by Dr. A. M. Goldthorpe and Dr. S. T. Pybus (*Supplement*, July 28, p. 87). These letters have had some publicity recently in the lay press. There are many aspects of the Service which are contradictory to the glowing Guillebaud report. For example, recent statistics show that by far the greatest number of Health Service patients seek their family doctor's care for antenatal treatment. Public health authorities are rather "alarmed" about these facts. It is obvious that the vast sums of money squandered on public authority antenatal clinics might be at least curtailed. Other examples can easily be cited where facts prove that there is a great deal of unnecessary expenditure in the administration of the Service. How long is the doctor and his family to suffer our collective "kid glove" tactics with a Ministry persisting indefinitely in the Alice in Welfareland role? The B.M.A. will certainly have to reassess its powers (if these are not in its present constitution) to withdraw services and to plan for this type of action. Certainly the present situation warrants this all the more, and future troubles with a lay Minister may well make this an imperative decision. It is up to every medical practitioner to support B.M.A. action, and more especially is it true that every young graduate should seek its membership. It is very urgent indeed that the B.M.A. presents a tougher attitude to cavalier treatments and willy-nilly attitudes of Ministers, who are essentially, at any rate, party politicians. And is not the whole tempo of the N.H.S. (as we have come to experience it) in its gross inefficiencies due mainly to the considerations of party politics?—I am, etc.,

Birmingham. J. J. BROOKS.

SIR,—It is a pity that Drs. A. C. J. Saudek and H. P. Hilditch (*Supplement*, August 11, p. 100) should choose to stir up internal controversies at a time when it is vitally necessary for the profession to be completely united. It might have occurred to them that such unity is not likely to be achieved if thousands of those concerned are to be excluded from any benefits that may accrue from a successful fight on the remuneration issue. It is, of course, nonsense to suggest that the Minister's attitude is being determined by the methods that the profession chooses to distribute the available money, and any attempt at this point to forward sectional interests could only end in defeat for us all.

There are a number of fallacious statements in their letter which, through constant repetition, may be accepted as true unless they are actively contradicted. First, let it be firmly stated that large-list doctors do not, for the most part, have large incomes; relatively large maybe, but still small compared with those earned in other professions and in business. Most of them have commitments proportionate to the level of their incomes, and the inflation of recent years has placed many in a difficult financial position. Furthermore, they have not obtained their status by "head-hunting and poor standards of practice," but by hard work, ability, willingness to practise in undesirable areas, and reputations built up through the years. Finally, young doctors must realize that there is nothing new in having to make do on a small income in one's early years of practice. This was certainly the case when I first started; however, in those days it was the custom to get established first and get married afterwards, so that we did not suffer so much hardship.

Surely the thing to realize is that all of us, young and not quite so young, general practitioners and consultants, established and unestablished, are all relatively hard up, and that we must concentrate all our energies and thoughts to the common good. Otherwise we shall certainly get nowhere at all and we shall have to consider giving up medicine for some more remunerative occupation or, at any rate, taking good care that our sons do not follow in our footsteps.—I am, etc.,

Margate M. CURWEN.

SIR,—Our profession appears once again to be meekly accepting the adroit handling of the Minister of Health, aided and abetted by his lay staff. The Negotiating Committee, having talked of firm action, is now in conclave working out legal arguments which should provide the Minister with debating points for many months to come. Further, it is holiday time and Parliament does not reassemble until October, so why rush? Our esteemed *Journal* even tells us to enjoy our holiday. Among associates one begins to detect an attitude of "The Minister has done it again, and wangled out of commitments as in previous times." This easy acceptance, surprisingly enough, comes from practitioners who are the first to grumble about their compensation and the many inadequacies of the Service but once more seem to be mildly bending their heads to the ministerial yoke.

I suggest we decide whether, in the light of present conditions and previous authoritative promises, we consider increased remuneration justifiable and necessary. If the answer is yes, then we should not allow the Minister to dilly-dally but should tell him we insist on a proper scale of payment being made. This must date from April, 1956, and must be accepted within one month. If the Minister is on holiday then his staff, who answered so off-handedly before, can do his thinking for him and implement our proposals. If we are not united in this purpose then we waste our time, but if we are then we should have a definite line to follow to ensure results. The British Medical Association should advise all area secretaries to call branch meetings in September, and, again provided the profession considers its claim reasonable, I suggest the following points be voted on: (1) The profession should give one month's notice of their intention to stop issuing National Insurance certificates. (2) If after one month of refusal to issue certificates our claim has not been met the profession should give a stated time, say four months, after which there should be mass resignation from the Service. In the meantime the public be warned of this likelihood and insurance companies approached to try to work out some insurance scheme for general health purposes. There would be no question of refusal to treat anyone who was ill.

The opportunity should also be taken to make the Minister and his Civil Service advisers realize that the profession are the important workers of the Health Service, and that, while the public is the first consideration, the profession comes next, and the ministerial staff a very low third. In this way we can control our own affairs and make sure the doctor knows of any advances, schemes, or changes before the public. We do not begrudge the Minister his television appearances, but we should control them when medical matters are involved.

I agree that many improvements are necessary in the general running of the health scheme, and also in the method of remuneration, but our first consideration at present should be the implementation of our claim and the insistence on control of the working of the scheme. Any alterations in the present National Health scheme system can then be made by a united profession striving to reach an efficient peak of service, both from the doctor's and from the patient's point of view.—I am, etc.,

Luton, Beds. ANDREW JACKSON.

SIR,—The newspapers and our own P.R.O. tell us that we, as G.P.s, receive an average net income of £2,222. Some of us are mystified, as we only have the evidence of our

quarterly cheques to guide us, and they seem to tell a different story.

In front of me I have a quarterly statement from our executive council concerning a colleague, not in my partnership. His figures read as follows:

	£	s.	d.
List of 2,164 at 4s. 3d.	459	17	0
Loading	125	0	0
Superannuation	37	8	10
Temporary residents	11	1	0
Total	633	6	10

This equals £2,533 7s. 4d. per annum gross.

The practice expenses incurred are not likely to be less than 30% of this figure, which gives a net income of roughly £1,774. Now the point of interest to all of us is: What happens to the very substantial difference? Most of us in working-class practice have no private work.—I am, etc.,

Harrow. J. W. SIMPSON.

SIR,—I noticed in Sir Anthony Eden's broadcast he mentioned the sum of £70 million compensation that Colonel Nasser had promised to pay to the Suez Canal Company when he nationalized the canal. The Prime Minister has no faith in this being paid. I do not think he has much to criticize on this score when you consider the £66 million still due to the medical practitioners after 10 years of nationalization. All we get is a meagre 2½% interest, and income tax is deducted from this. It would appear that the Egyptian president is taking a leaf out of the Government's book. I suggest that the Prime Minister should clear his own debts before criticizing others.

I hold no brief for Colonel Nasser, as I dislike Fascists and Communists as much as any other man, but I did want to draw your attention to Sir Anthony's statement. Maybe some use could be made of it in the negotiations. —I am, etc.,

Huddersfield. H. W. DAVIS.

SIR,—Each week the letters in your columns regarding the remuneration claim stimulate many of us to almost fighting pitch, but frustration follows when no action results. I suggest that the B.M.A. forms an "action committee" which must decide on some form of token strike—e.g., refusal to sign National Insurance certificates. Ballot forms should be sent to all doctors concerned, and, if the method is approved by the majority of us, it should be implemented without delay. It seems that some form of token strike is needed and many of us are only awaiting a decisive directive as to how and when. Let the B.M.A. give it soon. —I am, etc.,

Harold Wood, Essex. C. R. LYNN.

SIR,—The Minister of Health and his Scottish colleague appear to have timed their reply to our claim (if such it can be dubbed) with some care, so as to postpone the inevitable clash between the profession and the Government. Is it not possible for us to turn the Ministers' dilatoriness to our advantage? I submit that, by affording us more time, the Ministers have offered us the opportunity of strengthening our case, and that we would be most ill-advised not to take advantage of this.

In the first place, we can now launch a vigorous national publicity campaign disabusing the public of the widely held view that we are already well off and only making an unnecessary and unjustifiable fuss. This should be conducted through the media of press, radio, and television. We could also strengthen our bargaining position in two ways. We could, in the next two months, make a formal and urgent approach to the representative bodies of other professions, with a view to bringing into play collective pressure in excess of that possible with our meagre numbers, pledging mutual support between the professions; and we could initiate a nation-wide effort to become somewhat less dependent on the Government for our livelihood (and there are ways of achieving this which are perhaps best left unpublished at present).

Finally, we can prepare a definite, albeit flexible, schedule of measures to be brought into play in its entirety or piecemeal, as the Ministers' attitude demands, each measure applicable to an anticipated obstructive manœuvre on the part of the Government. As I see it, without such a plan we are doomed to being out-generalled by Ministers who have at hand not only the big guns but the inclination to turn them on us.

Is it not possible, Sir, for the Council of the B.M.A. to consider these with the other suggestions that have been made, to institute immediate emergency action, and, above all, to inform the profession what manner of additional armaments it has been possible to muster, before joining battle in October? Failure to seize this opportunity now cannot but jeopardize our negotiating committee's position in two months' time.—I am, etc.,

Upton, Hunts. JOHN K. PATERSON.

Emergency Call Service

SIR,—Recently the Duke of Edinburgh, when he opened the Study Conference on Human Problems in Industry, said: "It may not be very easy to decide what we are aiming at in this modern world of ours, but whatever the target we must take into account that all people are primarily citizens, and not just workers with a bit of private life."

The present-day G.P. is a worker with about as much private life as a battery hen. Our patients also are not over-contented with things as they are. How often does a patient get "tided over for the night" with some tablets, when he would have much preferred a visit? Since the G.M.S. Committee has condemned the Emergency Call Service, I wonder if an alternative scheme would be acceptable. The public health services have been evolved to meet the needs not met adequately by other agencies, and until recently were always in a constant state of extension and development. A salaried night service, run by the public health authorities, would no more be in competition with the family doctor than the present school medical service. Indeed, it might well be initially recruited from doctors in the school medical service assisted by the health visitors.

Why cannot the London Emergency Call Service be regularized and expanded on the above lines, and the whole country enjoy its advantages?—I am, etc.,

Caterham, Surrey. D. S. PORTER.

Health Centres

SIR,—I would like to express my pleasure at the report of the London Local Medical Committee (*Supplement*, August 4, p. 89), for I am in complete agreement with their conclusions. In my opinion the only intelligent method of conducting general practice these days under the National Health Service is from a health centre. It is only in this way that our full potentialities in the realm of preventive medicine—surely our ultimate aim—can be realized.

Most of the recommendations in the report are already in effect at the William Budd Health Centre, which was built by the Bristol local health authority and has been running since July, 1953. Here I must say that, despite some early misgivings from our colleagues, we have had every help and encouragement from the local authority and especially from the medical officer of health, Dr. R. C. Wofinden. The building is of modest proportions, doctors are consulted over all staff appointments, and they work in close co-operation with the health visitors and other local authority workers who use the consulting-room suites in the afternoons. The doctors hold their own infant welfare and antenatal sessions at the centre. The reason why doctors outside the centre are not invited to share in these facilities is quite simple. The centre is fully occupied daily from 8 a.m. to 8 p.m., and it would just not be possible to hold any further sessions. The answer is for outside doctors to get together and agitate for more health centres.

Group partnerships in which there is a limited amount of specialization have their advantages, but at the William Budd the absence of such a partnership is not found to be

in any way a drawback. Doctors do see each other's patients in emergency and call each other into consultation over puzzling or interesting cases.

Under the National Health Service Act the health centres, of course, must be provided by the local authority. I am afraid that the loan scheme for group practice will not attract more than a few groups of doctors. After all, we have to buy our own houses, and that means a capital investment of between £3,000 and £4,000, and I feel sure most doctors would be unwilling or unable to invest any more money into group practice buildings. On the other hand, the local authorities could take over and convert large houses in built-up areas at minimal expense.

The doctors at the William Budd pay only a nominal rent, and that, in my opinion, is as it should be. We are not engaged in "business" nor does the better service we provide increase our remuneration, although it takes up far more of our time. Physicians and surgeons working in hospitals do not pay for their consulting-rooms, theatres, and so on. Unfortunately we are too often bedevilled by the question of costs, and yet the balance sheet can be most misleading. The William Budd on that score looks expensive to run, but the money is spent for the most part on wages and salaries of people who would be doing that work anyway, and in premises which would otherwise be empty for many hours each day. The allocation of costs between the general practitioner and local health authority branches of the service is purely nominal on a two-thirds to one-third time-user basis, but in fact is quite unrealistic, for such is the integration achieved that it is impossible to separate the two on a proper actuarial basis. It is also impossible to assess the benefit to the patients from what is undoubtedly a higher standard of medical service.—I am, etc.,

Bristol, 4. J. SLUGLETT.

Subsistence Allowances

SIR,—Will you allow a very old member to comment on the recent A.R.M.? I have read the accounts of the meeting with interest, but regret some of the decisions come to, and particularly the vote in favour of subsistence allowances (*Supplement*, July 14, p. 15). Some of the arguments put forward in support are far from convincing. I cannot think that the quality of representation, or the democratic foundation, is threatened. The meeting itself contradicts any such fear, for there is said to have been keenness on the part of representatives, both young and elderly, and the speaking was on a high level. This does not suggest difficulty in enlisting suitable representatives, or any reluctance to serve. The chairman of the Organization Committee spoke of many men and women ready to sacrifice their time and energies in the work of the Association, and this applies to representatives as well as to those engaged in other activities; and may this happy position long remain.

I ask: Is it necessary to upset the finances of the Association by this new expense? So as not to seem entirely obstructive I suggest that a Division wishing to contribute towards its representative's expenses could do so through a local voluntary fund, many of which already exist. One speaker proposed an allowance of two guineas per day, and on the present basis of representation that means less than 5s. per member, which should be willingly subscribed.—I am, etc.,

Sheffield. HENRY BROWN.

Board and Lodging Charges

SIR,—Recently the appropriate Medical Whitley Council has agreed that board and lodging charges for resident medical officers be standardized at all grades throughout the country (*Supplement*, August 11, p. 99). For senior house officers—of which I am one—the sum is £150 per annum.

I further understand that no abatement is allowable on account of annual leave. In spite of this, in some hospital groups the residents are rebated while on holiday. I have benefited from this in the past. Now I am in a group where the rebate is not allowed. This is according to regulations, and one cannot object. However, I do query the fact that locumtenents are also having their board and lodging subtracted. This means that this hospital is not only taking from each S.H.O. post at £150 per annum but an extra £15 from the locum—a total of £165. If by chance the senior house officer decides not to take a holiday I wonder how the hospital explains that it has only extracted £150 from the post—or if he does take a holiday and gets a locum, does the extra £15 go down as "capital gains"? At any rate, it does not seem to me to be a "fair deal." I would be very grateful if anyone can enlighten me.—I am, etc.,

London, N.W.1. W. M. E. TWEED.

A Pathologist's Pay

SIR,—Dr. A. S. Nicholas (*Supplement*, August 4, p. 95), who entered his family business instead of trying to specialize, chose the better part. He was lucky to have so readily available an alternative to the prospects of the registrar grades. His analysis, made in 1952, remains accurate, with the amendment that the decline in the purchasing power of our salaries has accelerated since then.

The position of a registrar in any specialty is grim. Pathology, at one time one of the least crowded, is now rapidly filling up, and the position in general medicine and surgery should be too well known to require re-emphasis. Many of us, by the time we reach senior house officer or registrar status, desire to marry, and some are so rash as to have children. The married registrar must face life in rented accommodation for several years, as moves are too frequent to make house purchase practicable, even if the capital can be borrowed. Such accommodation is hard to find in our larger cities, often unsuitable for young children, and ruinously expensive. In addition, the family must face at least three moves, for a change of post often involves a change of residence.

Prospects of ultimate advancement do not compensate for these immediate hardships. That of achieving consultant status is poor, and is governed by a sum so simple that it does not seem to have entered the calculations either of the Ministry, which is only to be expected, or of our own Association, which might be presumed to give some thought to its younger members. Each consultant has an assistant, of one or other of the trainee grades. It takes at the most ten years to pass through all the trainee grades and attain the recommended age for consultant status. But most consultants can be expected to hold their posts for thirty years, from age 35 to 65. Therefore, each consultant is training three successors for his own post. I have yet to hear any creditable explanation of what happens to the other two.

The favoured position of Dr. Nicholas and our other contemporaries "in business" needs no emphasis. They have their expense accounts and "company" cars, and often assistance with removal expenses and financing of house purchase. Some even get assistance with their children's school fees. It is obvious that the young doctor is valued by the community at less than the commercial traveller, and much less than the production engineer. The corollary is also obvious; in a few years' time there will be a lot more competition for the post of commercial traveller, and a lot less for that of trainee specialist. The first-class men will not be content to subsist, and see their families subsist, at a lower standard of living. Medicine will not attract first-class men to second-class pay and third-class prospects; a worth-while, interesting job, and service to the community, are satisfying things, but they do not pay the rent, let alone for a car.

There seem to be two ways out of the impasse; out of the profession for which we have been trained, or out of the country. Dr. Nicholas has testified to the former, and a large number of your correspondents during the last two years have borne witness to the latter. Many of my contemporaries have been in the latter group, and next month I am taking their advice and emigrating to Canada. I

understand that in the Dominion the conscientious practice of medicine is rewarded by a standard of living not widely different from that of the average commercial traveller.—I am, etc.,

Birmingham, 15. H. E. EMSON.

Economy in the N.H.S.

SIR,—I hope that the advisers to the Minister of Health and the Secretary of State for Scotland will take note of the excellent advice given by Dr. H. Wilson (*Supplement*, August 11, p. 101).

Why should we, as doctors, be trammelled with the responsibility of saving Government money? Why should we be obliged to make ourselves unpopular for the sake of the Government? Our concern must be with therapeutics. The cost involved is a matter which should be arranged between the patient and the State. In other words, it is a political problem.

Several years ago, in a letter in your columns, I advocated that a list of essential medicines should be drawn up and that only those drugs should be supplied free. A doctor would prescribe what he thought fit, but the patient would pay for anything not on the list. The list of free drugs would be reviewed frequently and revised according to current opinion. A scheme such as this would create no real hardship and I feel sure would be willingly accepted by the people. Local medical committees would be relieved of the need to scrutinize their fellow practitioners' prescriptions and would apply themselves rather to the constructive work of recommending to the central committee which drugs should be added from time to time to the "free list." This would evoke stimulating discussions on practical therapeutics in place of the unrewarding, exasperating, and often futile investigation of high prescribing costs.

Much the same can be said of the ambulance service. Prior to 1948 our local nursing association financed an ambulance and car service. It was not abused, because the committee defined clearly which type of case should have a free ambulance or car. Doubtful cases were brought before the committee and rulings were established for subsequent usage. The service given was efficient and economical. Nowadays cars are not used for transporting patients in my area. If a patient requires transport an ambulance must be used, although we all know that a car is often suitable and always more economical; and yet, at the same time, we are constantly exhorted to economize.

The shilling tax and the Cohen Committee reports have both failed in their intended purpose, but they clearly indicate that the Government no longer accepts the "free for all" principle in the National Health Service. The way then is clear for another step along the lines suggested. I am convinced that this would bring economy as well as a worth-while improvement in the Service.—I am, etc.,

Fife. JAMES B. FLEMING.

Charging Each Other

SIR,—In a letter received some weeks ago from the British United Provident Association there occurs this statement: "In the conditions of to-day, however, we find that medical men often receive accounts from their colleagues, more particularly where services are rendered to dependants." Elsewhere in the same communication one notes that "dependants" are defined as (1) wife or husband, (2) all children under 18.

A few years ago when I offered a fee to a specialist he said with some show of indignation: "It has come to something if we have to make a living out of each other." And it is indeed deplorable if we have now come to that. One would like to think that this business of charging each other fees, which is akin after all to making a living by taking in each other's washing, is only practised by some of the younger members of the profession who have little respect for what one has always regarded hitherto as part almost of the Hippocratic Oath.—I am, etc.,

Brighton. G. L. DAVIES.

Association Notices

SIR CHARLES HASTINGS AND CHARLES OLIVER HAWTHORNE CLINICAL PRIZES, 1957

The Sir Charles Hastings Clinical Prize Competition is established by the Association for the promotion of systematic observation, research, and record in general practice. The competition has been extended by the addition of a second prize known as the Charles Oliver Hawthorne Clinical Prize. The following are the regulations governing the awards:

1. The Sir Charles Hastings Clinical Prize, consisting of a certificate and £75, will be awarded for the best entry.

2. The Charles Oliver Hawthorne Clinical Prize, consisting of a certificate and £50, will be awarded for the second best entry.

3. Any member of the Association who is engaged in general practice is eligible to compete for these prizes.

4. The work submitted must include personal observations and experiences collected by the candidate in general practice, and a high order of excellence will be required. If no work entered is of sufficient merit no award will be made. Candidates in their entries should confine their attention to their own observations in practice rather than to comments on previously published work on the subject, though reference to current literature should not be omitted when it bears directly on their results, their interpretations, and their conclusions.

5. Essays, or whatever form the candidate desires his work to take, must be sent to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, not later than December 31, 1956.

6. A prizewinner in any year is eligible for an award of either of the prizes in any subsequent year. A study or essay that has been published in the medical press or elsewhere will not be considered eligible for a prize, and a contribution offered in one year cannot be accepted in any subsequent year unless it includes evidence of further work.

7. If any question arises in reference to the eligibility of the candidate or the admissibility of his or her entry the decision of the Council on any such point shall be final.

8. Preliminary notice of entry for this competition is required, on a form of application to be obtained from the Secretary.

9. Each entry, which should be unsigned, must be typewritten or printed on one side of the paper only and accompanied by a note of the candidate's name and address.

10. No definite limits are laid down as to the length of the work submitted, but the Council anticipates that for this competition 3,000 to 10,000 words would be suitable.

11. Inquiries relative to the prizes should be addressed to the Secretary.

OCCUPATIONAL HEALTH PRIZE

The Occupational Health Prize was established by the Association for the purpose of encouraging interest and research in the field of occupational health. The Council of the British Medical Association is prepared to consider the award of this prize, which consists of a certificate and £50, in the year 1957. Any member of the Association who is engaged in the practice of occupational health, either whole-time or part-time, is eligible to compete for the prize. Candidates may select their own subject.

Entries should be submitted in a form suitable for publication and must include personal observations and experiences collected by the candidates in the course of their work. If no entry is of sufficient merit no award will be made. Candidates should confine their attention to their own observations rather than to comments on previously published work on the subject, though reference to current literature should not be omitted when it bears directly on their results, their interpretations, and their conclusions.

Essays, or whatever form the candidate desires his work to take, must be sent to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, not later than January 31, 1957. No study or essay that has been published in the medical press or elsewhere will be considered eligible for the prize, and a contribution

offered in one year cannot be accepted in any subsequent year unless it includes evidence of further work. A previous prizewinner is not precluded from entering. If any question arises in reference to the eligibility of the candidate or the admissibility of his or her essay, the decision of the Council on any such point shall be final.

Preliminary notice of entry for this competition is required on a form of application to be obtained from the Secretary. Each entry must be typewritten or printed on one side of the paper only, and accompanied by a note of the candidate's name and address. No definite limits are laid down as to the length of essays, but the Council anticipates that, for this competition, essays should consist of between 3,000 and 10,000 words. Inquiries relative to the prize should be addressed to the Secretary.

PRIZE ESSAY COMPETITION FOR PROVISIONALLY REGISTERED PRACTITIONERS, 1957

The Council of the British Medical Association is prepared to consider the award, in 1957, of prizes to provisionally registered practitioners for essays submitted in open competition. The subject of the essay is: "Medicine is an Art as well as a Science."

In awarding the prizes due regard will be given to evidence of personal observation and experience. No study or essay that has previously appeared in the medical press or elsewhere will be considered eligible for a prize.

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A message to all parents about children's feet

by C. & J. CLARK LTD*

THERE has been a lot in the papers lately about 'Healthy Feet' and many suggestions have been made that the only really healthy shoes for children to wear are those made *entirely* of leather. It is claimed that only by wearing all-leather shoes can the child's foot breathe easily and that soles of rubber and newer materials cause hot feet, swelling, etc. ¶Now these statements can be very misleading. We make some two million pairs of children's shoes every year. Some are all leather, some have soles of rubber and newer materials—all have leather insoles and all have leather uppers. It is true that leather 'breathes' and the largest proportion of perspiration passes through the uppers. It is also true that leather is not waterproof and that damp coming through the soles can cause harm to the foot and cold in the head. ¶After over a hundred and thirty years of shoe making and many thousands of tests, the great majority of our shoes are made with leather uppers, leather insoles (on which the foot rests) and 'Solite' or rubber final soles, because these are non-slip, long wearing and waterproof. ¶We now quote from an article by an Orthopædic Surgeon, recently published in the 'Leather Trades Review':

"The ideal shoe from the foot health point of view, of course, is the shoe constructed entirely of leather with a fine covering of composition on the sole and heel, for the purposes of wear. It can be argued that putting a film of synthetic material over a leather sole would prevent the passage of air or perspiration from the foot. But in fact that is not entirely true for tests we have made (at a London teaching hospital) show that the largest proportion of perspiration passes through the uppers."

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Elastoplast Airstrip

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Waterproof yet non-occlusive, this new Adhesive first-aid dressing PREVENTS MACERATION

Elastoplast Airstrip is made from a specially developed plastic material which is not perforated but consists of a microporous extensible filter. Sweat and skin exudates evaporate through this air-permeable dressing at the same rate as they develop on the skin. At the same time this new dressing is waterproof, preventing water, grease and oil from coming in contact with the wound.

Airstrip allows the wound to "breathe"; therefore maceration cannot develop. Because the surface of the wound and surrounding skin remain dry, the dressing can be left on until the wound heals—which it does under ideal dry conditions.

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The air-permeable Elastoplast Airstrip dressing prevents development of maceration. Healing takes place in minimum time.

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ABSTRACTS OF WORLD MEDICINE

offered in one year cannot be accepted in any subsequent year unless it includes evidence of further work. A previous prizewinner is not precluded from entering. If any question arises in reference to the eligibility of the candidate or the admissibility of his or her essay, the decision of the Council on any such point shall be final.

Preliminary notice of entry for this competition is required on a form of application to be obtained from the Secretary. Each entry must be typewritten or printed on one side of the paper only, and accompanied by a note of the candidate's name and address. No definite limits are laid down as to the length of essays, but the Council anticipates that, for this competition, essays should consist of between 3,000 and 10,000 words. Inquiries relative to the prize should be addressed to the Secretary.

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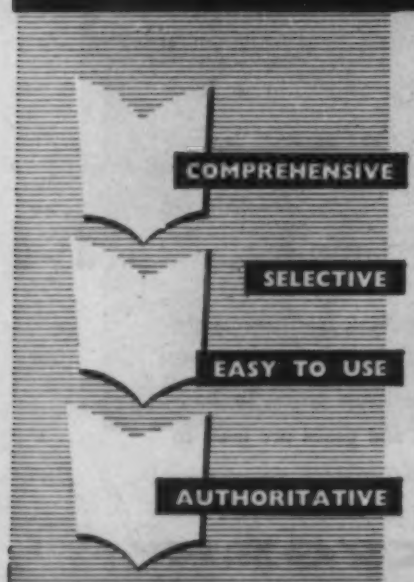

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BRITISH MEDICAL ASSOCIATION

B.M.A. House, Tavistock Square, London, W.C.1

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Applicants should state name, address, age, nationality, qualifications, and enclose (unless otherwise specified) one copy each of 3 recent ★ testimonials with short statement of experience and appointments held.

Applications should be sent at once if no closing date is given.

Canvassing in any form will disqualify.

★*SERVICE MEMBERS may have difficulty in supplying recent testimonials, but this should not deter them from applying.*

A fully registered medical practitioner who is liable for National Service must obtain de'erment of recruitment in writing from the Central Medical Recruitment Committee or (in Scotland) the Scottish Central Medical Recruitment Committee before accepting any civilian appointment.

The position of provisionally registered medical practitioners who are liable for National Service has been made clear in a notice sent to them by the Ministry of Labour and National Service.

SALARY SCALES OF JUNIOR GRADES OF HOSPITAL MEDICAL STAFF

Registrar Grades, Whole-time

(*a*) *REGISTRAR:* Posts obtained normally not less than two years after registration as a medical practitioner and held normally for two years: £850 per annum in the first year; £965 per annum in the second and any subsequent years.

(*b*) *SENIOR REGISTRAR:* Posts obtained normally not less than four years after registration as a medical practitioner and held normally for four years; £1,100 per annum in the first year; £1,200 per annum in the second year; £1,300 per annum in the third year; £1,400 per annum in any subsequent years.

Other Grades, Whole-time

(*a*) *HOUSE OFFICERS:*

(i) *Provisionally registered medical practitioners:* £425 per annum for the first post held; £475 per annum for the second and all subsequent posts held;

provided that the employing authority (subject in the case of a Hospital Management Committee to the consent of the Regional Hospital Board) shall have discretion to determine that the remuneration of any officer holding his first post in the National Health Service as a House Officer shall be £475 per annum if they are satisfied that the officer has held at least one hospital post outside, of not less than six months' duration, involving clinical responsibilities equivalent to those of house posts in the National Health Service and supervised by appropriate specialist staff.

(ii) *Fully registered medical practitioners:* £525 per annum for any post held;

provided that in exceptional circumstances, subject to the consent of the Minister, this rate may be exceeded by up to £50 per annum where a post cannot be filled otherwise.

In each case under sub-sections (i) and (ii) above, a deduction of £125 per annum in respect of board and lodging and other services provided shall be made and each post shall be tenable for six months.

(*b*) *SENIOR HOUSE OFFICER:* Posts obtained normally not less than one year (in Scotland, two years) after registration as a medical practitioner and normally held for one year only: £745 per annum.

(*c*) *JUNIOR HOSPITAL MEDICAL OFFICER:* Officers who have held house appointments but who are not Registrars and who have less responsibility than other hospital officers of non-consultant status: £775 (for an officer appointed not less than one year after full registration as a medical practitioner) by £50 to £1,075 per annum.

ALL NATIONAL HEALTH SERVICE HOSPITAL APPOINTMENTS ARE IN ACCORDANCE WITH THE TERMS AND CONDITIONS OF SERVICE OF HOSPITAL MEDICAL STAFF

Those intending to apply for resident appointments in the Registrar grades are recommended to make inquiries with regard to the deductions proposed for board and lodging at the time of submitting their applications, where this is not stated in the advertisement.

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Medicine
Neurosurgery
Obstetrics and Gynaecology
Ophthalmology
Orthopaedics
Paediatrics
Pathology
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Plastic Surgery
Psychiatry
Radiology
Rheumatology
Surgery
Thoracic Surgery
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PRACTICES (Executive Councils)

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BURSCOUGH, Ormskirk

Applications invited for vacancy (urban and rural) due to death. List at present approximately 2,700. Residence including surgery may be available. There is also a branch surgery. Apply on form E.C. 16A before September 8, 1956, to Jos. A. Speed, Clerk of the Lancashire Executive Council, 42, West Cliff, Preston. (7378)

DENTON, near Manchester

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PRACTICES (Offered)

MIDDLESEX, SUBURB. NON-N.H.S. PRACtice for disposal. Income about £5,000 per annum. Details from M.P.A.B., B.M.A. House, Tavistock Square, W.C.1.

PRACTICES (Exchange)

NORTH LONDON RESIDENTIAL SUBURB, singlehanded 2,100 N.H.S. units, income £2,200 per annum, no midwifery, freehold house; requires Bournemouth only, £1,500 minimum, singlehanded. For details apply Medical Practices Advisory Bureau, B.M.A. House, Tavistock Square, London, W.C.1.

PRACTICES (Wanted)

T.C.D. GRADUATE, 44. M.D., F.R.C.P.I., requires medical practice or partnership, 1957.—Box PR.1263, B.M.J.

WOMAN DOCTOR (47) NOW IN SUBURBAN practice would like to hear of opening, coast or country, within next 1-2 years.—Box PR.1459, B.M.J.

PARTNERSHIPS (Wanted)

EXPERIENCED G.P. & OBSTETRICS AND hospital, married, returning England end August from Canada, requires partnership with, without, succession. Town or Country. Capital available house purchase.—Box PA.1473, B.M.J.

EXPERIENCED G.P., AGED 39, SEEKS Partnership after preliminary trial period. Available November.—Box PA.1382, B.M.J.

ASSISTANTSHIPS VACANT

Wanted, Assistant, male or female, London. Good salary and prospects by arrangement. Appointment, now or near future. Accommodation available.—Box A.1467, B.M.J.

Wanted, Assistant, outdoor, car essential, rota. London west.—Box A.1465, B.M.J.

Wanted, Assistant, Male or Female, Pleasant Midland Town. Car essential. Salary £1,000 plus £100 car allowance.—Box A.1475, B.M.J.

Wanted, October, Female Assistant for Rural District of Wensleydale, North Yorkshire. Good Salary, Car allowance, no view.—Apply Box A.1477, B.M.J.

Wanted, London, W.C. district, part-time Assistant. Agreed remuneration, plus furnished house (3 rooms, etc.), for Saturday morning surgery and some visits.—Box A.1489, B.M.J.

Wanted, outdoor Assistant (married), industrial practice. Salary £1,100 per annum, including car allowance. Free house and garage. View later.—Box A.1353, B.M.J.

Wanted, part-time Assistant (single) for rota night duties once weekly, central London, accommodation offered, suit P.G.—Box A.1452, B.M.J.

Wanted very soon, outdoor male Assistant, Surrey town, car owner. Salary £1,000 per annum, plus £150 car allowance.—Box A.1377, B.M.J.

Assistant wanted, probable view, partnership practice. Car owner.—Box A.1466, B.M.J.

Assistant wanted in Hampshire, Salary £1,000. No view. No accommodation.—Box A.1455, B.M.J.

Assistant with view Junior Partnership required Plymouth area. Capital required for house purchase. State experience, age, etc.—Box A.1451, B.M.J.

Assistant, married, Scottish graduate required for partnership near North-East Coast. Duties to begin November 1, 1956. Salary, including car allowance, £1,050 per year, together with free house and rates.—Apply Box A.1476, B.M.J.

Doctors required for Night Duties. North London area. Car provided. Good remuneration. G.P. experience essential. 'Phone: TUD 0203.

Jewish Assistant wanted with early view partnership, possibility eventual succession. University town, 50 miles London. House for sale.—Box A.1488, B.M.J.

Large mixed practice, N.W. London, offers Assistantship with view. Unfurnished flat and garage available. Applicant must have car, and capital to buy house ultimately. Salary £1,000. £150 car allowance.—Box A.1461, B.M.J.

ASSISTANTS AVAILABLE

Assistantship with or without view. Married, Protestant, car owner, 31. Hospital experience plus midwifery. R.N. North England, Scotland preferred. Available mid-October. Completing traineeship.—Box A.1456, B.M.J.

Assistants Available—contd.

Assistantship, with or without view. Leeds graduate. 32. Family. Hospital. G.P. Car.—Box A.1457, B.M.J.

Experienced woman practitioner seeks full- or part-time Assistantship. Car owner.—Dr. Ettlinger. BAY 5449.

Ex-Warrior M.B., B.S., M.R.C.S., L.R.C.P., D.R.C.O.G. (36). Surgery, Obstetrics, Casualty, Gynae., own Hospital; Locum and Trainee. View sought Partnership/succession. Country town S.E. line Wash Southampton. Car. Capital for house.—Box A.1485, B.M.J.

M.B., B.S. (London), D.R.C.O.G., 32, seeks assistantship with view. Hospital and G.P. experience. Married. Car. Southern England preferred.—Box A.1474, B.M.J.

Woman Doctor, 34, Requires Assistantship southern half England. Ten years' experience, own car.—Box A.1460, B.M.J.

York or near, Assistantship with view or prospects, now or within 2 years. M.B., Ch.B. (Ed.), 1948. Five years G.P. Age 35, married, car. Good references.—Box A.1468, B.M.J.

TRAINEE GENERAL PRACTITIONERS (Vacant)

St. Thomas's Principal offers Trainee vacancy in very pleasant rural practice.—Box T.1371, B.M.J.

Trainee, either sex, central London, live out. Car provided.—Box T.1453, B.M.J.

Trainee wanted, early October, male, married or single, car owner. Cambridge. Light duties. Furnished flat available.—Box T.1470, B.M.J.

Trainee wanted, mid-September, male, Protestant. Salary £775, car £150. Live out.—Dr. McLeod, City Park, St. Andrews.

Trainee, single, Car owner and post national service preferred. Busy partnership, pleasant Midland town. References please. Excellent opportunity.—Box T.1478, B.M.J.

Trainee required, residential district, S.E.27.—Box T.1487, B.M.J.

LOCUMS (Vacant)

Wanted, experienced Locum, single male, car owner, midwifery, sole charge from October 5 to 14 inclusive. Usual terms.—Dr. Manning, 1, Wogan Road, Pembroke. Tel. 234.

Wanted, Locum, male or female, for practice in Southend-on-Sea, Essex, from September 16 to October 7. Car available.—Apply Box L.1479, B.M.J.

Wanted, Locum, experienced male, first fort-night September, North Wales. No collieries. Own car desirable.—Dr. Martin, Penmachno, Bettws-y-Coed.

Wanted, Locum, car, week-end commencing soon Friday, August 31. Live in. Six guineas.—Dr. Pougher, George Street, Leamington.

Wanted, October 18 to 26, Locum small rural practice E. Midlands. No midwifery.—Box L.1480, B.M.J.

Locum for compact Birmingham practice, any fortnight in September or October. Live out. Car desirable. Tel. Calthorpe 2253.

Locum required from October 4 for three weeks. Country town, partner remaining.—Box L.1363, B.M.J.

Locum required immediately for three weeks. Partnership practice. Semi-rural. Car available.—Dr. Howe, Park Street, Ripon. Tel. 117.

Locum required with car, Kilteorn House, Nantwich, any fortnight as soon as possible.

Lady Doctor, Hammersmith, requires Locum fortnight September. Easily run practice, no midwifery.—Box L.1481, B.M.J.

Reliable Locum required for September 16 to October 7. East Coast.—Box L.1469, B.M.J.

Hammersmith Hospital & Institute of Obstetrics and Gynaecology
Du Cane Road, London, W.12

Locum Registrar

(non-resident) required for one month from September 1. Age, qualifications, experience, names two referees, to Secretary, Board of Governors, immediately. (7291)

Royal Northern Hospital, Holloway, N.7

Locum Resident Anaesthetist (S.H.O.)

required September 3 to 14 inclusive. Applications to Hospital Secretary. (7329)

Wandsworth Hospital Group

Locum Registrar (Obstetrics & Gynaecology)

required from September 21 until permanent appointment made. Duties at St. James' Hospital and Weir Maternity Hospital. Applications giving full particulars to Group Secretary, St. James' Hospital, S.W.12, by September 8. (42739) (7282)

Alton, Hants., Henry Gauvain Hospital

Locum Registrar (General Surgery and Orthopaedics)

required early in September. Applications as soon as possible to the Secretary, Henry Gauvain Hospital, Alton. (7256)

Ayr, Glengall Mental Hospital (710 beds)

Applications are invited from qualified Practitioners for post of

Locum Junior Hospital Medical Officer

(resident or non-resident) at Glengall Mental Hospital, Ayr, as from September 1, 1956. Salary in accordance with National Health Service Conditions of Service. Applications, with copy of testimonials, to be submitted to Medical Superintendent, Glengall Mental Hospital, Ayr. (7380)

Bedford General Hospital (439 beds)

Locum Anaesthetic Registrar

required three months commencing September or shorter period. Salary £17 10s. per week. Applications and testimonials, to Group Secretary, Bedford Group H.M.C., 3, Kimbolton Road, Bedford. (6031)

Birmingham Royal Orthopaedic Hospital (242 beds)

Whole-time Locum Tenens Assistant Orthopaedic Surgeon (S.H.M.O.)

Duties also at associated hospitals and clinics. Vacant, minimum 4 months. Salary 31½ gns. per week. Applications to S.A.M.O., 10, Augustus Road, Birmingham, 15. (7185)

Black Notley Hospital, Braintree, Essex

Locum Registrar in Orthopaedic and Renal Tuberculosis

required from October 1 to 28, 1956. Applications to the Group Secretary, Colchester H.M.C., 14, Pope's Lane, Colchester, Essex. (7265)

Croydon Group Hospital Management Committee

Mayday Hospital

Locum Tenens Medical Registrar

Whole-time, September 19 to October 12 inclusive. Non-resident. Previous experience in General Medicine essential. Applications in writing, giving age, experience, and names of two referees, to Geo. A. Paines, Group Secretary, Croydon Hospital Management Committee, General Hospital, London Road, Croydon. (7129)

Essex County Hospital, Colchester

Locum Radiologist (Consultant or Senior Hospital Medical Officer Grade)

required immediately for a period up to 6 weeks, for duties at hospitals in the Colchester Group. Applications to Group Secretary, Colchester H.M.C., 14, Pope's Lane, Colchester, Essex. (7266)

Guildford Hospital Management Committee

St. Luke's Hospital, Guildford

Locum Obstetric & Gynaecological Registrar

required immediately. Applications to Physician Superintendent. (7381)

Ipswich and East Suffolk Hospital
Anglesea Road Wing

Locum Tenens Casualty Officer

Senior House Officer grade, required from October 2 to October 31, 1956. Applications with full particulars to Hospital Secretary. (7186)

Lancaster Moor Hospital, Lancaster (Regional Mental Hospital)

Locum Assistant Psychiatrist (S.H.M.O.)

Locum S.H.M.O. required immediately for several weeks. Previous psychiatric experience essential. Salary according to national scales and at present 31½ guineas per week less residential charges. Accommodation for single person only. Apply Medical Superintendent. (6740)

Royal Sussex County Hospital, Brighton

A full-time Locum Registrar in Orthopaedic Surgery

required from September 3, 1956, for approximately four weeks (preferably resident). Applications stating usual particulars, with names and addresses of two referees, to be forwarded to the Group Secretary, Brighton & Lewes Hospital Management Committee, Royal Sussex County Hospital, Brighton. (7357)

St. Albans City Hospital
St. Albans, Herts (384 beds)

Locum Tenens Anaesthetic Registrar

resident, required for the period September 10 to 23 inclusive. Applications to Secretary, Mid-Herts Group Hospital Management Committee, Beak House, Catherine Street, St. Albans. (7187)

St. Albans City Hospital
Normandy Road, St. Albans (384 beds)

Locum Tenens Surgical Registrar

required for one of the two general surgical teams for the period September 10 to 30 inclusive. Applications to the Secretary, Mid-Herts Group Hospital Management Committee, Beak House, Catherine Street, St. Albans. (7188)

St. Heller Hospital, Carshalton, Surrey

Locum Anaesthetic Registrar

wanted for 14 weeks from September 17. Hospital recognised for D.A. and F.F.A. Applications giving qualifications and previous experience, to Group Secretary at above address. (7130)

Sheffield Regional Hospital Board

Locum for Consultant Physician

required for Boston Group of hospitals and Grantham for period September 9 to 29. Remuneration according to status. Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, naming two referees. (7134)

Sheffield Regional Hospital Board

Locum Medical Registrar

required at City General Hospital, Sheffield, from September 24 for approximately 10 weeks. Apply Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, naming two referees. (7131)

Sheffield Regional Hospital Board

Whole-time Locum Assistant Radiologist

required September 1 for the Derbyshire Royal Infirmary. Remuneration according to status. Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, naming two referees. (7132)

Sheffield Regional Hospital Board

Locum Resident Registrar (Orthopaedics)

required. Scunthorpe and District War Memorial Hospital for period August 27 to September 23. Remuneration £17 10s. per week. Apply Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, naming two referees. (7133)

Sidcup and Swanley Hospital Management Committee

Locum Resident Surgical Officer

required for four months from September 21, 1956. Rate of pay £17 10s. per week. Applicants should be widely experienced as a considerable amount of emergency surgery is required. Applications to Secretary, Queen Mary's Hospital, Sidcup, Kent. (7333)

Southend, General Hospital

Locum Casualty Officer (Senior House Officer Grade)

required for the period September 1 to October 21, 1956, inclusive. Two other Casualty Officers are employed. Applications to be sent to the undersigned as soon as possible.—J. C. Field, Secretary. (7356)

South-Western Regional Hospital Board

Locum Consultant Obstetrician & Gynaecologist

required to September 9, 1956. Applications, giving qualifications and experience, and names of two referees, to the Secretary of the Regional Hospital Board, 27, Tyndalls Park Road, Bristol, 8, immediately. (7358)

LOCUMS (Available)

Available Locums. Partnership or sole charge. Own car. Live in.—Box L.1462, B.M.J.

London pre-registration doctor available as Locum House Officer, preferably surgical.—Box L.1458, B.M.J.

SITUATIONS (Vacant)

Dr. Barnardo's Homes

Two Women Medical Officers

required as follows: (a) Attached to Headquarters staff. Chief duties visiting and inspection of branch homes and supervision of foster children's medical records. (b) House Officer at the Australasian Hospital and Village Home, Barkingside. Salary scale £750 to £1,150. Posts vacant October 1. For further details apply to Chief Medical Officer, 18, Stepney Causeway, London, E.1. (6809)

SITUATIONS (Wanted)

Overseas Rheumatologist requires opening in Rheumatology in Great Britain or Ireland.—Box S.1379, B.M.J.

APPOINTMENTS

ANAESTHETICS

NEWCASTLE REGIONAL HOSPITAL BOARD

Gateshead District Hospital Management Committee Area
(Main hospitals: Queen Elizabeth (176 beds) Bensham General (230 beds), Dunston Hill (300 beds))

CONSULTANT ANAESTHETIST

whole-time or maximum part-time for nine notional half-days per week. Applications, with names and addresses of three referees, to S.A.M.O., Walker Gate Hospital, Benfield Road, Newcastle-upon-Tyne, 6, within 28 days. (7189)

N.E. METROPOLITAN REGIONAL HOSPITAL BOARD

ANAESTHETIC REGISTRAR (Resident)
St. Andrew's Hospital, Bow, E.3
Recognized for F.F.A. & D.A.

ANAESTHETIC REGISTRAR
(Resident or Non-resident)
King George Hospital, Ilford, Essex
Recognized for F.F.A. & D.A.

ANAESTHETIC REGISTRAR (Non-resident)
Whipps Cross Hospital, Leytonstone, E.11
Recognized for F.F.A. & D.A.

Appointments subject to review after one year. Application forms from Secretary, 11a, Portland Place, W.1, to be returned by September 8. (7348)

LEEDS REGIONAL HOSPITAL BOARD

REGISTRAR IN ANAESTHETICS

Halifax Group (approximately 290 beds in the Surgical Specialties). Resident. Applications, stating age, qualifications and details of present and previous appointments (showing dates), together with the names and addresses of three referees, to the Secretary, Joint Registrars Committee, Park Parade, Harrogate, by September 7, 1956. (7190)

MANCHESTER REGIONAL HOSPITAL BOARD

SENIOR REGISTRAR IN ANAESTHETICS

with duties in the North Manchester Group of Hospitals (mainly at Crumpsall Hospital) and at Booth Hall Hospital. F.F.A. desirable. Arrangements may later be made for the person appointed to transfer to the United Manchester Hospitals. Application forms, obtainable from the Senior Administrative Medical Officer of the Board, Cheetwood Road, Manchester, 8, should be returned by September 3, 1956. (7314)

SHEFFIELD REGIONAL HOSPITAL BOARD and BOARD OF GOVERNORS OF THE UNITED SHEFFIELD HOSPITALS

RECIPROCAL TRAINING SCHEME FOR SENIOR REGISTRARS

Whole-time Senior Registrar in Anaesthetics required. Initial tenure at City General Hospital, Sheffield (692 beds), a large general hospital having teaching affiliations with the University of Sheffield and with Professorial Medical and Gynaecological Units, a Department of Thoracic Surgery and a Regional Cardiological Centre. Appointment for one year in first instance and renewable thereafter annually. Incumbent will be transferred to the Teaching Hospitals for the second phase of the appointment in accordance with arrangements under the Reciprocal Training Scheme. Renewal of appointment and transfer to the Teaching Hospitals will be subject to satisfactory work and progress. Further details and form of application from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood Road, Sheffield, 10. Forms to be returned by September 3, 1956. (6916)

THE BOARD OF GOVERNORS OF THE UNITED BRISTOL HOSPITALS AND THE SOUTH-WESTERN REGIONAL HOSPITAL BOARD

Applications are invited by the above Boards from registered medical practitioners for the joint appointment of

REGISTRAR IN ANAESTHETICS

This post becomes vacant on November 1, 1956. The appointment will be held for one year in the first instance, and be renewable for a further year. The successful candidate will be appointed to work for the first year mainly at Southmead Hospital, Bristol, but may also be required to undertake duties at other hospitals in the Group. Southmead Hospital is recognized for the purpose of taking the examination for the Fellowship of the Faculty of Anaesthetists. Applications, stating date of birth, qualifications, and experience, together with the names and addresses of two referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park Road, Bristol, 8, not later than September 10, 1956. (7359)

THE UNITED BIRMINGHAM HOSPITALS and THE BIRMINGHAM REGIONAL HOSPITAL BOARD

Applications are invited for two Joint Appointments of

SENIOR REGISTRAR IN ANAESTHETICS
(Non-Resident)

In these two new appointments facilities will be available for training and experience in Anaesthesia for Neurosurgery, Plastic Surgery and Thoracic Surgery in addition to general anaesthetic duties, and time will be equally divided between the two Boards.

(1) Neurosurgery, plastic surgery and general anaesthetic duties in the Queen Elizabeth Hospital and other hospitals in the Teaching Group and thoracic surgery at Hill Top, Yardley Green and St. Wulstan's Hospitals.

(2) Neurosurgery, plastic surgery and general anaesthetic duties in the Queen Elizabeth Hospital and other hospitals in the Teaching Group and general anaesthetic duties at Little Bromwich General Hospital, in which is a centre for the treatment of poliomyelitis cases with respiratory involvement, and other regional hospitals.

Possession of the Two-Part Diploma in Anaesthetics of the Conjoint Examining Board of England or the Diploma of Fellow of the Faculty of Anaesthetists of the Royal College of Surgeons of England would be desirable. Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned to him not later than September 8, 1956. (7299)

SOUTH CHESHIRE HOSPITAL MANAGEMENT COMMITTEE

J.H.M.O. (Anaesthetics)

3 years' appointment; D.A. preferred. New operating suite to be opened shortly. Duties chiefly at general hospital and a Maternity Unit at another hospital. Hospital approved for D.A. Salary and conditions as per regulations. Applications, giving age, details of experience, and names of three referees, immediately to Group Secretary, Group Headquarters, Barony Hospital, Nantwich. (7029)

DULWICH HOSPITAL
East Dulwich Grove, London, S.E.22

Applications invited for appointment as

SENIOR HOUSE OFFICER (Anaesthetist)

Vacant from September 17, 1956. Recognized for F.F.A.R.C.S. and D.A.; the hospital is associated with King's College Hospital Medical School for undergraduate teaching purposes. Applications, stating age, qualifications, and experience, enclosing copy testimonials or names of two referees, to the Group Secretary, Camberwell H.M.C., Dulwich Hospital, East Dulwich Grove, S.E.22. Last day for receipt of applications September 5. (7191)

NELSON HOSPITAL
Kingston Road, Merton, S.W.20

RESIDENT ANAESTHETIST
(Senior House Officer Grade)

Applications, stating age, experience and qualifications, with copies of testimonials, and the name of one referee, should be sent to the Group Secretary, St. Helier Hospital, Carshalton, Surrey. (7136)

WOOLWICH GROUP HOSPITAL MANAGEMENT COMMITTEE

SENIOR HOUSE OFFICERS (Anaesthetics)

One at St. Nicholas Hospital, Plumstead, and one at Memorial Hospital, Woolwich, vacant immediately. Both posts recognized for F.F.A.R.C.S. or D.A. and are for 6 months in the first instance and may be renewed. Apply to Group Secretary, Memorial Hospital, Shooters Hill, Woolwich, S.E.18. (7255)

BIRMINGHAM, 18, DUDLEY ROAD HOSPITAL (700 beds)

SENIOR HOUSE OFFICER (Anaesthetics)

required. Resident. (Recognized for D.A. and F.F.A.R.C.S.) Extensive experience of Anaesthetics not necessary. Duties include list and emergency work in General Surgery, Gynaecology, Obstetrics and E.N.T. at Hospitals in Group. Vacant October 21, 1956. Detailed applications, with copies of three recent testimonials, to Group Secretary. (7355)

BIRMINGHAM, 29, SELLY OAK HOSPITAL (955 equipped beds)

SENIOR HOUSE OFFICER (Anaesthetics)

Resident/non-resident. Residential charge £150 per annum. Apply Medical Superintendent, with detail of qualifications, experience, age and copies of three recent testimonials. (7215)

DUDLEY, THE GUEST HOSPITAL (154 beds)

SENIOR HOUSE OFFICER (Anaesthetics)

Post now vacant. Apply, Group Secretary, Guest Hospital, Dudley. (7052)

DARLINGTON MEMORIAL HOSPITAL

RESIDENT ANAESTHETIST S.H.O.

Applications are invited from male or female practitioners for the above appointment, vacant September. The Hospital is recognized for the study for the D.A. and F.F.A.R.C.S. Salary £745 per annum. Apply with references and full details to the undersigned forthwith.—G. W. Beckwith, Group Secretary. (7114)

ESSEX COUNTY HOSPITAL, Colchester (188 beds)

Applications invited for post of

SENIOR HOUSE OFFICER (Anaesthetics)

Post tenable for 1 year. Recognized for F.F.A. and D.A. The successful candidate will be called upon to give anaesthetics in other hospitals in the Group. Applications, with copies of three testimonials, to Group Secretary, Colchester H.M.C., 14, Pope's Lane, Colchester, Essex. (7267)

FARNBOROUGH HOSPITAL, Kent (800 beds)

SENIOR HOUSE OFFICER in Anaesthetics required immediately for one year. Recognized for D.A. and F.F.A. R.C.S. Apply, stating age, qualifications (with dates) and experience and naming three referees, to Administrative Officer. (7337)

ILFORD AND BARKING GROUP HOSPITAL MANAGEMENT COMMITTEE

There will be a vacancy for a

SENIOR HOUSE OFFICER Anaesthetist

at the King George Hospital, Ilford, on October 1, 1956. The Officer appointed will be required to be available for duty in other Hospitals in the Group. Salary will be at the rate of £745 per annum, less £150 per annum emoluments. Applicants should have been registered not less than one year, and should send applications accompanied by copies of three testimonials to the undersigned within seven days of the appearance of this advertisement.—H. F. Harris, Group Secretary, King George Hospital, Ilford. (7162)

KETTERING & DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Kettering General Hospital, Kettering (170 beds)

Applications are invited from registered medical practitioners for the appointment of

SENIOR HOUSE OFFICER in Anaesthetics

Post recognized for D.A. Applications giving details of qualifications and experience and enclosing copies of three recent testimonials to be sent to the Group Secretary at the above address. (6835)

NOTTINGHAM GENERAL HOSPITAL

SENIOR HOUSE OFFICER (Anaesthetics)

required as soon as possible. The post is recognized for the D.A., and the F.F.A.R.C.S. This is a busy general Hospital giving experience in all branches of surgery. Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary. (5642)

ORPINGTON HOSPITAL, Orpington, Kent

RESIDENT S.H.O. Anaesthetist

required immediately for above 813 bedded General Hospital. Male or female. Recognized for D.A. Applications, with copies of two recent testimonials, to Physician Superintendent. (7062)

ROYAL DEVON & EXETER HOSPITAL, Exeter

Applications are invited from registered Medical Practitioners for the appointment of

SENIOR HOUSE OFFICER (Anaesthetics)

resident or non-resident. Vacant now. The post is recognized for the F.F.A.R.C.S. Examination. Applications, with copies of two recent testimonials, to the Hospital Secretary. (7241)

SEDGEFIELD GENERAL HOSPITAL
Sedgefield, Stockton-on-Tees, Co. Durham (336 beds)

(Sedgefield Hospital Management Committee)

SENIOR HOUSE OFFICER Anaesthetist

urgently required. Full consultant staff employed and the post, which offers excellent facilities for Anaesthetic training, is recognized in connection with examinations for the higher qualifications. Applications, together with two recent testimonials, or names of two referees, to the undersigned.—L. Watson, Group Secretary. (7089)

STAFFORD HOSPITAL MANAGEMENT COMMITTEE

SENIOR HOUSE OFFICER (Anaesthetics)

Male or female. Resident. Recognized for D.A. Applications to Group Secretary, Stafford H.M.C., 13, Foregate Street, Stafford. (7192)

WORCESTER, RONKSWOOD HOSPITAL

RESIDENT ANAESTHETIST (S.H.O. status)

required at end of September for post which is recognized by the Faculty of Anaesthetists. Duties cover all specialties. Married accommodation available. Applications, with names and addresses of three referees, to be sent to the Hospital Secretary. (7360)

Anaesthetics—contd.

NORTHAMPTON GENERAL HOSPITAL
(482 beds)

Vacancy October 1, 1956, for
HOUSE OFFICER
Department of Anaesthetics. Recognized for D.A. Six months' appointment in first instance. Applications as soon as possible to S. G. Hill, Superintendent. (7137)

BACTERIOLOGY

WESTERN REGIONAL HOSPITAL BOARD

Applications are invited for the following appointment, which will be for one year in the first instance:

REGISTRAR in Bacteriology
based at the Royal Infirmary, Glasgow. Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of three referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent Street, Glasgow, C.2, by September 8, 1956. This appointment is subject to the National Health Service (Scotland) (Superannuation) Regulations. (7361)

CASUALTY

LIVERPOOL REGIONAL HOSPITAL BOARD
Warrington Group

Applications are invited for the post of
WHOLE-TIME SENIOR CASUALTY OFFICER
in the above group with duties mainly at Warrington Infirmary. Applicants should possess a higher qualification in Surgery. The successful candidate will be required to take charge of the Casualty department and undertake certain duties in the Orthopaedic Department. The appointment will be for a period not exceeding four years. Salary determined by age and experience within the range £1,475 to £2,025. Forms of application from, and to be returned to, Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James Street, Liverpool, 2, to be received not later than September 15, 1956.—Vincent Collings, Secretary to the Board. (7369)

NEWCASTLE REGIONAL HOSPITAL BOARD

Tees-Side Hospital Management Committee
(Population 350,000)
Stockton and Thornaby Hospital (130 beds)

SENIOR CASUALTY OFFICER
whole-time. Duration of tenure of post not exceeding four years. Salary within the range £1,475 to £2,025 per annum. The Senior Casualty Officer will be required, subject to the supervision of the Senior Surgeon to General Surgical Clinic No. 3 and the Senior Orthopaedic Surgeon, to organise the work of the busy Casualty Department. The Senior Casualty Officer must reside near the Stockton and Thornaby Hospital. Further particulars may be obtained from the Senior Surgeon, General Surgical Clinic No. 3, at the Stockton and Thornaby Hospital, Stockton-on-Tees. Applications, with names and addresses of three referees, to be forwarded to Deputy Senior Administrative Medical Officer, Newcastle Regional Hospital Board, Walker Gate Hospital, Benfield Road, Newcastle-upon-Tyne, 6, within 28 days. (7216)

HUDDERSFIELD ROYAL INFIRMARY
(285 beds)

Applications are invited for the post of
CASUALTY OFFICER
The post, which is resident, is recognized under the Fellowship regulations and will be graded either J.H.M.O. or S.H.O. according to experience. Duties terminate at 7 p.m. daily with one night weekly on call. Applications for the appointment, which will be vacant on October 1, 1956, should be accompanied by copies of three recent testimonials and addressed to the undersigned.—H. J. Johnson, Group Secretary, The Royal Infirmary, Huddersfield. (6511)

SOUTHPORT GENERAL INFIRMARY

JUNIOR HOSPITAL MEDICAL OFFICER
(resident). Whole-time casualty post vacant about November. Apply stating age, qualifications, experience, nationality, enclosing copies of two recent testimonials, to Group Secretary, Southport & District H.M.C., Promenade Hospital, Southport. (7317)

CONNAUGHT HOSPITAL
Walthamstow, E.17 (118 beds)

Applications are invited for the post of
SECOND CASUALTY OFFICER
with duties in the Department of Orthopaedic and Traumatic Surgery (Senior House Officer grade), recognized for F.R.C.S. Salary £745 per annum, less £150 per annum for board, lodging, etc. Applications, with full details and copies of two recent testimonials, should be sent immediately to Secretary, H.M.C. Forest Group, Langthorne Road, E.11. (7193)

IMPORTANT NOTICE
APPOINTMENTS

Medical practitioners are requested

not to apply

for any appointment specified in this notice or for any appointment under an authority referred to in this notice without first communicating with the Secretary of the British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, or in the case of the Irish appointment, with the Medical Secretary of the Irish Medical Association, 10, Fitzwilliam Place, Dublin, or in the case of the South African appointment, with the Medical Secretary of the Medical Association of South Africa, 35, Wale Street, Capetown, to learn the views of the Association regarding the terms and conditions of service pertaining to the appointment:

COUNTY BOROUGH OF MIDDLESBROUGH

REPUBLIC OF IRELAND.
PORTIUNCULA HOSPITAL,
BALLINASLOE, CO. GALWAY
Visiting Staff.

GOVERNMENT OF CYPRUS

MINES BENEFIT SOCIETY,
JOHANNESBURG
Appointment of Urologist.

By Order of the Council,

A. MACRAE,

August 21, 1956. Secretary.

BOW GROUP HOSPITAL MANAGEMENT COMMITTEE

SENIOR HOUSE OFFICER
required at Poplar Hospital, East India Dock Road, E.14. Duties are mainly in connection with the Receiving Room and Casualty Departments. Preference will be given to a candidate who is preparing for a higher qualification. Applications to the Group Secretary, 2a, Bow Road, E.3. (7312)

HAMPSTEAD GENERAL HOSPITAL
Haverstock Hill, N.W.3
(Royal Free Hospital Group)

Applications are invited from registered Medical Practitioners for the post of
RESIDENT CASUALTY OFFICER
(graded as Senior House Officer). Salary £745 per annum. Tenable for a period of six months at the Main Out-patients Department, Bayham Street, N.W.1. Application forms may be obtained from the Secretary, to whom they should be returned, together with copies of three recent testimonials, by September 5, 1956. (7321)

ROYAL NORTHERN HOSPITAL
Holloway, N.7

Applications are invited for the post of
CASUALTY OFFICER (S.H.O. grade)
with duties in the E.N.T. department, vacant September 17, 1956. Post recognized for F.R.C.S. Applications to be sent to the Hospital Secretary by September 4, 1956. (7247)

WANSTEAD HOSPITAL, Harrow Hill, E.11
(191 beds)

Applications are invited for the post of
CASUALTY OFFICER (recognized for F.R.C.S.)
graded Senior House Officer, vacant September 5, 1956. Salary £745 per annum, less £150 per annum for board, lodging, etc. Applications, with full details, and copies of two recent testimonials, to be sent immediately to Secretary, H.M.C., Forest Group, Langthorne Road, E.11. (6881)

DUDLEY, THE GUEST HOSPITAL (134 beds)

SENIOR HOUSE OFFICER (Casualty)
Post now vacant. Apply, Group Secretary, Guest Hospital, Dudley, Worcs. (7054)

EPSOM DISTRICT HOSPITAL
Dorking Road, Epsom, Surrey

SENIOR HOUSE OFFICER (CASUALTY)
required October 1, 1956. Post non-resident, recognized for F.R.C.S. Twelve months' appointment. Busy Casualty and Out-patient Department with excellent experience in Minor and Traumatic Surgery. Candidates should have held previous House Officer Posts. Applications, stating age, qualifications, experience, with copies of two recent testimonials, should be sent as soon as possible to Group Secretary at above address. (7194)

LEEDS (A) GROUP HOSPITAL MANAGEMENT COMMITTEE

Applications are invited from registered medical practitioners for the appointment of
CASUALTY OFFICER (Senior House Officer)
at the Public Dispensary and Hospital, Leeds, 2. Modern Casualty Department dealing with 50,000 initial attendances per annum. The appointment is recognized by the Royal College of Surgeons for Fellowship. Applications to the undersigned as soon as possible.—J. Folkard, Secretary to the Committee, Administrative Offices, St. James's Hospital, Leeds, 9. (7195)

NORTHAMPTON GENERAL HOSPITAL
(482 beds)

Vacancy October 1, 1956, for
SENIOR HOUSE OFFICER
Casualty Department, to work in conjunction with another Casualty Officer. Recognized for F.R.C.S. Six months appointment in first instance. Applications as soon as possible to S. G. Hill, Superintendent. (7138)

NOTTINGHAM GENERAL HOSPITAL

Applications are invited from Registered Medical Practitioners for the post of
SENIOR HOUSE OFFICER (Casualty)
duties to commence on or about September 7. Establishment 3. Recognized for F.R.C.S. Post offers wide experience of Casualty work. Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Secretary, General Hospital, Nottingham. (7140)

SOUTH SHIELDS INGHAM INFIRMARY
(188 beds)

CASUALTY OFFICER
(Senior House Officer or Pre-registration)
required for duty on September 24, 1956, to work under supervision of Senior Casualty Officer. Post recognized by Royal Colleges. Applications to House Governor and Secretary. (7343)

SOUTH-WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE

West Middlesex Hospital

SENIOR HOUSE OFFICER
required for Admissions and Casualty Department. Must have held medical and surgical post. Applications to Group Secretary, West Middlesex Hospital, Isleworth, by September 4, 1956. (7344)

THE LEICESTER ROYAL INFIRMARY

Applications are invited for two posts of
SENIOR HOUSE OFFICER (Surgical)
for a new Casualty Department. Duties will consist of six months as Senior House Officer, Casualty, and six months as Senior House Officer in General Surgery. The posts are recognized for the F.R.C.S. Applications, stating age and qualifications, together with copies of recent testimonials, to the Group Secretary, No. 1 Hospital Management Committee, The Leicester Royal Infirmary, by September 8. (7177)

UNITED BRISTOL HOSPITALS

Royal Infirmary Branch

Applications are invited for the resident post of
SENIOR CASUALTY HOUSE SURGEON
(Senior House Officer grade)
tenable from October 1, 1956, for six months in the first instance. Applications, giving age, qualifications and experience, and names and addresses of two referees, should be sent by Monday, September 3, 1956, to: Secretary to the Board, Royal Infirmary Branch, Bristol, 2. (7362)

QUEEN MARY'S HOSPITAL FOR THE EAST END
West Ham Lane, Stratford, London, E.15

JUNIOR CASUALTY OFFICER
(House Officer 3rd Post)
required immediately for six months. Applications, with copies of testimonials, to Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15, by August 28, 1956. (7035)

READING, BATTLE HOSPITAL (391 beds)

Applications are invited from registered medical practitioners for the post of
RESIDENT JUNIOR HOUSE SURGEON
in the Area Accident and Orthopaedic Department. Post vacant October 1 next. F.R.C.S. recognized. Also casualty duties. Salary £425 to £525 per annum, less £125 board-residence. Apply, stating age, qualifications with dates, nationality, present post with one copy of recent testimonial, to Hospital Secretary. (7341)

IMPORTANT: All intending applicants should read the revised NOTICE at the top of page 28

Casualty—contd.

CHESTERFIELD HOSPITAL MANAGEMENT COMMITTEE

CASUALTY OFFICER

required towards mid-September at Chesterfield Royal Hospital. Post recognized for pre-registration service and F.R.C.S. examinations. Appl., M. H. Boone, Secretary. (Pr.6921)

NORTHAMPTON GENERAL HOSPITAL (482 beds)

Vacancy October 1, 1956, for

HOUSE OFFICER

Casualty Department, to work in conjunction with Senior House Officer, Casualty Department. Recognized for F.R.C.S. and for medical pre-registration. Six months' appointment in first instance. Applications as soon as possible to S. G. Hill, Superintendent. (Pr.7139)

ROYAL SUSSEX COUNTY HOSPITAL (312 beds)

CASUALTY HOUSE SURGEON (one of three) required early September. Duties include work in Orthopaedic and Traumatic Unit. Recognized for pre-registration and F.R.C.S. Applications, stating usual particulars, and naming two referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7. (Pr.7092)

CHEST AND TUBERCULOSIS

(see also THORACIC SURGERY)

BROMPTON HOSPITAL, S.W.3

Applications invited for post of

MEDICAL REGISTRAR (Whole-time)

Salary within the Registrar grade. The appointment is for one year, commencing October 1, 1956, with eligibility for re-appointment. Candidates must hold the M.R.C.P. Diploma or the M.B. of a University. Applications, stating age, qualifications (with dates), nationality and appointments held, together with copies of testimonials, by September 8, to Kenneth A. F. Miles, House Governor. (7080)

ALTON, HANTS, LORD MAYOR TRELOAR ORTHOPAEDIC HOSPITAL

Applications invited from registered medical practitioners for post of whole-time

ORTHOPAEDIC REGISTRAR

Post provides experience in non-pulmonary tuberculosis and general orthopaedics and includes attendances at peripheral clinics. House available for married man and quarters for single man. Visit to hospital welcomed. Apply Secretary for form. (7294)

ALTON, HANTS, LORD MAYOR TRELOAR ORTHOPAEDIC HOSPITAL

Required immediately

LOCUM ORTHOPAEDIC REGISTRAR

for holiday duty, probably three months, post provides experience in non-pulmonary tuberculosis and general orthopaedics. Accommodation for single man now, for married man possibly later. Visit to Hospital welcomed. Apply Secretary. (7295)

WIGAN AND LEIGH AND WRIGHTINGTON GROUPS OF HOSPITALS

REGISTRAR IN CHEST DISEASES

Two busy chest clinics and opportunity to gain experience in Thoracic Surgical Unit. Applications, together with the names of two referees, to the Secretary, Wigan and Leigh Hospital Management Committee, Knowsley House, Wigan, as soon as possible. (7250)

DEVENDEAN HOSPITAL Bear Road, Brighton, 7 (145 beds)

Applications are invited for the post of

JUNIOR HOSPITAL MEDICAL OFFICER

at the above Hospital for chest diseases. Salary £775 by £50 to £1,075 per annum. Applications, stating nationality and usual particulars, together with the names of two referees, should be sent to the Administrative Officer, Brighton General Hospital, Elm Grove, Brighton, 7, as soon as possible. (7093)

BIRMINGHAM (SANATORIA) GROUP HOSPITAL MANAGEMENT COMMITTEE

Applications are invited for the post of

JUNIOR HOSPITAL MEDICAL OFFICER

at West Heath Hospital, Reddal Road, Birmingham, 31 (210 Tuberculosis with observation beds). The successful applicant will reside at the above hospital (accommodation for single person only), and will be offered facilities for undertaking duties at the Birmingham Chest Clinic, Great Charles Street, Birmingham, 3. Applications, stating age, qualifications, training and experience, together with copies of three recent testimonials, should be addressed to the Group Secretary, Birmingham (Sanatoria) Group H.M.C., Yardley Green Hospital, Birmingham, 9. (7254)

READING & DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Applications are invited for the appointment of

JUNIOR HOSPITAL MEDICAL OFFICER

in the Area Department of Diseases of the Chest, for duty in the Reading Chest Clinic. The post offers wide experience in both tuberculosis and non-tuberculous chest diseases and duties will include attendance at Prospect Park Hospital, Reading, and Peppard Chest Hospital, Henley. Facilities are available for post-graduate studies. Salary within the scale £775 to £1,075 per annum. Applications, stating age and qualifications, together with names of three referees, should be sent to the Group Secretary, 3, Craven Road, Reading. (6537)

SKIPTON (near), GRASSINGTON HOSPITAL (298 beds)

JUNIOR HOSPITAL MEDICAL OFFICER

required for the above hospital, which provides treatment for tuberculosis patients, men and women. Accommodation available for single applicants. Post tenable from September 1, 1956, or earlier if desired. Applications to Medical Superintendent. (6487)

THE LONDON CHEST HOSPITAL

Hospital for Diseases of the Chest

RESIDENT HOUSE SURGEON

required at the Hospital's Country Branch, near Hitchin and Letchworth, Herts. The post is graded as Senior House Officer and the appointment, which provides excellent opportunities for experience in thoracic surgery, is for six months. Applications from Registered Medical Practitioners, stating date of birth, qualifications (with dates) and previous appointments held, with copies of three testimonials, to be forwarded at once to the undersigned.—Thomas Brown, House Governor, London Chest Hospital, E.2. (7336)

MAIDSTONE, PRESTON HALL HOSPITAL British Legion Village, Maidstone, Kent

Applications are invited for the appointment of

SENIOR HOUSE OFFICER

Salary £745 per annum, national scale and conditions. The sanatorium contains 330 beds for the treatment of tuberculosis and includes a major thoracic surgical unit. Candidates may visit the hospital at any time. Applications, stating age, qualifications, and giving names of two referees, to be sent, not later than September 15, 1956, to A. A. Howick, Group Secretary. (7268)

NORTHAMPTON (near), CREATON SANATORIUM

Applications are invited from suitably qualified medical practitioners for the post of

SENIOR HOUSE OFFICER

The Sanatorium has 138 beds and is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a new major thoracic surgical unit for T.B. and non-tuberculous diseases of the chest. Applications, stating age, experience and qualifications, together with the names and addresses of two referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton. (6922)

WOODFORD GREEN, ESSEX, HARTS HOSPITAL (100 beds)

SENIOR HOUSE OFFICER

required. Post vacant October 4, 1956. The hospital is a modern sanatorium with a Thoracic Surgical Unit and Area Chest Clinic. The post offers exceptional opportunity for gaining experience in Tuberculosis and Diseases of the Chest. Accommodation for single person only. Salary £745 per annum, less £150 per annum for board, lodging, etc. Applications, with copies of two recent testimonials, should be sent immediately to Secretary, Forest Group H.M.C., Langhorne Road, E.11. (7141)

MIDHURST, SUSSEX, KING EDWARD VII SANATORIUM

Applications are invited for the appointment of

ASSISTANT MEDICAL OFFICER

Candidates should have had at least six months' experience of Tuberculous and Non-Tuberculous chest diseases. Commencing salary £600 per annum in addition to full residential emoluments. The post is superannuable. Applications, stating age, qualifications, experience and the names of three referees, should be sent to the Medical Superintendent and marked "A." (7269)

BROMPTON HOSPITAL, S.W.3

Applications invited for post of

RESIDENT HOUSE PHYSICIAN, 4 vacancies

Three vacancies for six months from November 1, 1956. Duties include work in Out-patient Department and Wards. One vacancy for nine months from November 1, 1956. The first three months at Brompton Hospital Sanatorium, Frimley, and the following six months at the Hospital in London covering work in Out-patient Department and wards. Salary at the rate of £525 per annum. Applications, stating age, qualifications (with dates), nationality and appointments held, together with copies of testimonials, by September 8, 1956, to Kenneth A. F. Miles, House Governor. (7297)

EDINBURGH CITY HOSPITAL

HOUSE PHYSICIAN (Male or Female)

required for T.B. Unit associated with Thoracic Surgical Unit and University Department of Tuberculosis and Diseases of Respiratory System. Six months' appointment, approved for pre-registration. Applications, with names of two referees, or copies of two recent testimonials, to Secretary, Board's Office, City Hospital, Greenbank Drive, Edinburgh. (Pr.7354)

NORTHAMPTON (near), CREATON SANATORIUM

Applications are invited for the post of

HOUSE OFFICER

which is recognized as a pre-registration medical appointment. The Sanatorium has 138 beds and is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a new major thoracic surgical unit for T.B. and non-tuberculous diseases of the chest. Applications, stating age, experience and qualifications, together with the names and addresses of two referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton. (Pr.6923)

DENTAL

THE ROYAL FREE HOSPITAL GROUP

Dental Department

RESIDENT DENTAL REGISTRAR

Applications are invited for the appointment of a full-time resident Dental Registrar to work under the general supervision of the visiting consultant Dental Surgeons. Duties would be of a varied nature including opportunities for surgical theatre work. The appointment is for one year in the first instance, duties to commence as soon as possible. Salary and conditions of service in accordance with the terms laid down by the Ministry of Health. Application should be made, stating qualifications, age and experience, and giving the names of three referees, to the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn Road, W.C.1, not later than September 15, 1956. (7322)

DERMATOLOGY

CAMBRIDGE, ADDENBROOKE'S HOSPITAL

DERMATOLOGICAL REGISTRAR

from October 8 for one year in the first instance, renewable for second year. Apply, with full particulars and names of three referees, to Secretary by September 8. (7196)

BIRMINGHAM, 15, THE SKIN HOSPITAL In-patients' Department, George Road

SENIOR HOUSE OFFICER or HOUSE OFFICER

according to experience. Modern well-equipped In-patients' Department, providing facilities for study of skin diseases. Required to assist Consultant at Out-patient Clinics. Applications, with copies of two recent testimonials, to Group Secretary, Dudley Road Hospital, Birmingham, 18. (7034)

BOARD OF MANAGEMENT FOR THE ABERDEEN GENERAL HOSPITALS

Applications are invited for the appointment of a

HOUSE PHYSICIAN

in the Skin and Dental Ward of the Aberdeen Royal Infirmary for a period of 6 months from August 1, 1956, to January 31, 1957. The post is a resident one. The appointment is approved as a pre-registration post and tenure for the prescribed period will count towards full registration on the *Medical Register* for provisionally registered practitioners. Applications, with full details, and giving the names of two referees, should be lodged immediately with the Secretary, Aberdeen General Hospitals, P.O. Box No. 92, 62, Queen's Road, Aberdeen. (Pr.7382)

EAR, NOSE, AND THROAT, ETC.

LONDON COUNTY COUNCIL

AUDIOLOGIST

required for sessional employment at various school treatment centres for the examination of deaf or partially deaf children. Applications invited from medical practitioners of consultant status. Fee 4 guineas a session of 1½ to 2½ hours. Apply for details and application form to the Medical Officer of Health (PH/D.1/1496), The County Hall, Westminster Bridge, S.E.1. (7248)

Ear, Nose, and Throat—contd.

OXFORD REGIONAL HOSPITAL BOARD

CONSULTANT in E.N.T. Surgery
(part-time, for eight sessions a week) to the High Wycombe/Aylesbury Area Department. Duties mainly at High Wycombe and Amersham. The successful candidate must reside in the area. Applicants should have had wide experience in the specialty and hold the F.R.C.S. or equivalent. Applications (10 copies) stating, age, qualifications, experience, and the names of three referees, should reach the Secretary, 43, Banbury Road, Oxford, by September 29, 1956. (7142)

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

PART-TIME CONSULTANT E.N.T. SURGEON (1 h.d.p.w.)
required for the Epsom (Surrey) Group. Duties mainly at Cobham and District Hospital. Applications by letter (5 copies) giving date of birth, qualifications, experience, three referees, to Secretary (S.1), S.W. Met. R.H.B., 11a, Portland Place, W.1, by September 22, 1956. Applicants may visit hospital by local arrangement. (7121)

BIRMINGHAM & MIDLAND EAR & THROAT HOSPITAL

REGISTRAR, E.N.T. SURGERY
Resident. Recognized for D.L.O. and F.R.C.S. Application forms from Group Secretary, Dudley Road Hospital, Birmingham, 18, to be returned by September 3. Candidates may visit hospital. (7197)

MANCHESTER REGIONAL HOSPITAL BOARD

Applications invited for post of
NON-RESIDENT REGISTRAR in E.N.T. Surgery
to the Salford and West Manchester Groups of Hospitals, with main duties at Salford Royal and Park Hospitals. Applications, together with names and addresses of two referees, to be sent to Group Secretary, Salford Royal Hospital, Salford, 3, before September 1, 1956. (7242)

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

CLINICAL ASSISTANT
required for one half-day a week (Wednesday afternoon) in the Ear, Nose and Throat Department of the West Herts Hospital, Hemel Hempstead. Salary £175 per annum. Post vacant immediately. Applications, giving details of experience, to Group Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth Road, Watford, Herts, by not later than 10 days after appearance of this advertisement. (7383)

BRIGHTON & LEWES HOSPITAL MANAGEMENT COMMITTEE GROUP HOSPITALS (78 beds)

SENIOR HOUSE OFFICER
for duties in the E.N.T. Department. Recognized for F.R.C.S. and D.L.O. Applications, stating usual particulars, together with the names of two referees, to be sent to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7. (7243)

GUILDFORD ROYAL SURREY COUNTY HOSPITAL (233 beds)

SENIOR HOUSE OFFICER
required for E.N.T. department. Post is recognized for the D.L.O. examination. Vacant September 17. Applications, with copies of three testimonials, should be sent as soon as possible to Hospital Secretary. (7270)

HULL (A) GROUP HOSPITAL MANAGEMENT COMMITTEE

Applications are invited for the post of
SENIOR HOUSE OFFICER
in the E.N.T. Department of the Victoria Hospital for Sick Children and the Hull Royal Infirmary. The post is recognized for the F.R.C.S. and D.L.O. Applications, with testimonials, should be sent to the Secretary, Victoria Hospital for Sick Children, Park Street, Hull. (7300)

NORTHAMPTON GENERAL HOSPITAL (482 beds)

Vacancy October 1, 1956, for
SENIOR HOUSE OFFICER
Ear, Nose, and Throat Department. Recognised for F.R.C.S. and for D.L.O. Six months' appointment in first instance. Applications as soon as possible to S. G. Hill, Superintendent. (7143)

THE LEICESTER ROYAL INFIRMARY

Applications are invited for the resident post of
SENIOR HOUSE OFFICER
to the Ear, Nose and Throat Department, for a period of 12 months commencing October 1. The post is recognized for the D.L.O. and F.R.C.S. Applications, stating age, qualifications and experience, together with copies of recent testimonials, to the Group Secretary, No. 1 Hospital Management Committee, The Leicester Royal Infirmary. (7198)

ROYAL SOUTH HANTS HOSPITAL, Southampton (274 beds) and SOUTHAMPTON GENERAL HOSPITAL (472 beds)

SENIOR HOUSE OFFICER (E.N.T.)
required beginning of October. This post is recognized for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. The Group includes a diagnostic and distributing Hearing Aid Centre. Applications, with copies of recent testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar Street, Southampton. (7281)

DARTFORD HOSPITAL MANAGEMENT COMMITTEE

HOUSE SURGEON (Specialty E.N.T.)
required at The Southern Hospital, Dartford, from September, 1956. The E.N.T. Department is recognized for the F.R.C.S. and the D.L.O. Dartford is of easy access to London, with a frequent train service. Residential accommodation might be made available for a married man. Applications to be sent to the Group Secretary, The Bow Arrow Hospital, Dartford, Kent. (7199)

TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE

North Riding Infirmary, Middlesbrough (Eye, Ear, Nose & Throat Centre)

Applications are invited for the post of
E.N.T. HOUSE OFFICER
The post is recognized for the D.L.O. examination and for the Fellowship in Otology of the Royal College of Surgeons. Applications, stating full details, and giving two names for reference, should be addressed to the Hospital Secretary. (7200)

GERIATRICS

EASTERN REGIONAL HOSPITAL BOARD (Scotland)
Geriatrics, Dundee and Angus Area

Applications are invited for the post of
SENIOR REGISTRAR
for the Geriatric Service in the Dundee and Angus Area, which is based on Maryfield (General Teaching) Hospital, Dundee, and Stracathro (General) Hospital, near Brechin. The Senior Registrar will have his main responsibilities at Stracathro Hospital. Further particulars and forms of application from the Secretary to the Board, 430, Blackness Road, Dundee, with whom applications must be lodged not later than September 8, 1956. (7014)

SWINDON & DISTRICT HOSPITAL MANAGEMENT COMMITTEE

CLINICAL ASSISTANTS, Geriatric Department
Applications invited for two posts of clinical assistant in Geriatric Department at St. Margaret's Hospital, Swindon (6 sessions per week divided between the two posts). Successful applicants will work under direction of Consulting Physician, and the appointments will be for a period of two years in the first instance. Remuneration at the rate of £175 per annum per session. Conditions of service in accordance with regulations for hospital medical and dental staff. Details of duties can be obtained from Group Secretary, 7, Okus Road, Swindon, to whom applications, giving names of three referees, should be sent by September 14, 1956. (7201)

WATFORD, SHRODELLS HOSPITAL (General Hospital, 420 beds)

Applications are invited for the post of
SENIOR HOUSE OFFICER
to the Geriatric Unit. This unit of 180 beds, under full-time Geriatrician, offers excellent clinical experience in the diagnosis and treatment of acute and other illnesses in the elderly. Full laboratory and radiological facilities available. Adequate time for reading. Applications, together with copies of not more than two testimonials, to reach the Medical Officer-in-Charge as soon as possible. (7048)

HAEMATOLOGY

UNITED MANCHESTER HOSPITALS

Manchester Royal Infirmary, Manchester, 13

SENIOR HOUSE OFFICER to the Department of Haematology
to commence as soon as possible. Whole-time, non-resident post. Appointment for six months, renewable for a second and possibly a third six months. Application form obtainable from the undersigned, to be returned not later than September 5, 1956.—G. H. Taylor, Secretary. (7271)

INFECTIOUS DISEASES

LEEDS (GROUP B) HOSPITAL MANAGEMENT COMMITTEE

Seacroft Hospital, Leeds

SENIOR HOUSE OFFICER in Infectious Diseases
required immediately. The Infectious Diseases Section, average bed occupancy 100 beds, is the I.D. undergraduate and postgraduate training unit and a Regional Centre for the treatment of poliomyelitis. The appointment is resident and for one year. Applications, stating age, nationality, qualifications, and experience, with names of three referees to whom reference may be made, to the Group Secretary, Seacroft Hospital, Leeds, 14. (7345)

MANCHESTER, 10, MONSALL HOSPITAL Newton Heath

SENIOR HOUSE OFFICER
required (resident) for infectious diseases wards. The hospital is a Regional Centre for Poliomyelitis. Applications, with names of two referees, to Deputy Group Secretary, Monsall Hospital, from whom further particulars may be obtained. (7301)

PLYMOUTH, THE SCOTT ISOLATION HOSPITAL

Plymouth Special Hospital Management Committee

SENIOR HOUSE OFFICER
Applications are invited for the above appointment from male registered medical practitioners who have preferably been qualified for one year and have had previous hospital experience. The applicant should be able to drive a car. The duties, in two departments, will be chiefly in connection with infectious and venereal diseases, the former including a substantial proportion of cases in children. The varied clinical work, including acute medical cases and early pulmonary tuberculosis, provides valuable experience, particularly to those reading for a higher medical degree. The appointment will be for one year, vacant on October 1 *next*. Applications, together with copies of two recent testimonials, should be sent to the Group Secretary, Plymouth Special Hospital Management Committee, 8, Nelson Gardens, Stoke, Plymouth, immediately. (7284)

MEDICINE

N.E. METROPOLITAN REGIONAL HOSPITAL BOARD

REGISTRAR in General Medicine & Paediatrics (Resident)
St. John's and Chelmsford & Essex Hospitals Chelmsford, Essex

Duties in Group Paediatric, Premature Baby and Neo-natal Departments and in the General Medical Wards of both Hospitals.

MEDICAL REGISTRAR (Resident or Non-resident)
St. Clement's Hospital, Bow Road, E.3.

Appointments subject to review after one year. Application forms from Secretary, 11a, Portland Place, W.1, to be returned by September 8. (7349)

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

Lambeth Hospital, Brook Drive, S.E.11

Applications are invited for the post of
MEDICAL REGISTRAR
vacant in November, 1956. The appointment will be for one year in the first instance. Preference will be given to applicants having a higher qualification in medicine. Canvassing will disqualify. Intending candidates are invited to visit the hospital. Forms of application (enclosing stamped addressed envelope) from the Secretary, to whom completed forms should be returned not later than September 8, 1956. (7144)

WELSH REGIONAL HOSPITAL BOARD

REGISTRAR IN GENERAL MEDICINE
based at Royal Alexandra Hospital, Rhyl (138 beds). May be required to visit other hospitals in Clwyd and Dyfrdwy H.M.C. area. Non-resident. Subject to review end of first year. Forms of application from S.A.M.O., Temple of Peace, Cathays Park, Cardiff, within 14 days. (7139)

IMPORTANT: All intending applicants should read the revised NOTICE at the top of page 28

Medicine—contd.

HENDON DISTRICT HOSPITAL
307, Hendon Way, Hendon, N.W.4

Applications are invited from General Medical Practitioners, whose practices are within Borough of Hendon, for appointment to the Medical Staff. Members of the Medical Staff have access to the general and private beds for the admission and treatment of their own patients and to such out-patient facilities as at present exist or can be provided by existing staff and accommodation. They may be required to undertake on later duties the treatment of patients admitted under emergency arrangements who are not patients of other members of the staff. Remuneration under paragraph 10(a) of Terms and Conditions. Further details may be obtained from the Hon. Medical Superintendent of the Hospital. Applications should be addressed to the Group Secretary, Hendon Group Hospital Management Committee, Edgware General Hospital, Edgware, not later than September 8, 1956. (7096)

MIDDLESBROUGH, POOLE HOSPITAL
Nunthorpe (Tuberculosis 208 beds)

Applications are invited for the appointment of
RESIDENT MEDICAL OFFICER
(married accommodation available) for general duties on medical and surgical wards (adults and children). The grading and salary of the appointment will be either that of J.H.M.O. or S.H.O. according to the experience of the candidate and will be subject in all respects to the National Conditions of Service. The hospital is a most modern one with an active thoracic surgery unit. Applications, stating age, nationality, qualifications and previous experience, and the names of three referees, to be sent immediately to the Group Secretary, Cleveland Hospital Management Committee, West Lane Hospital, Middlesbrough. (7342)

HITHER GREEN HOSPITAL
London, S.E.13

Lewisham Group Hospital Management Committee

Applications are invited for the post of
SENIOR HOUSE OFFICER
with duties in Infectious Diseases, General Medicine and E.N.T. Unit. Vacant October 1. The appointment is tenable for one year and may be either fully resident or resident only when on duty. Applications, stating age, qualifications and experience, with copy testimonials or names of referees, to Group Secretary, at Lewisham Hospital, S.E.13. (7202)

BANBURY, OXON, HORTON GENERAL HOSPITAL (163 beds)

SENIOR HOUSE OFFICER (Physician)
required beginning of September. Post provides experience in general medical and children's wards. Four other residents. Applications, stating age, nationality, qualifications, and names of two referees, to the Secretary. (6614)

BEVERLEY, YORKSHIRE, WESTWOOD HOSPITAL (229 beds)

HOUSE PHYSICIAN
House Officer or Senior House Officer grading according to experience. Vacant end of September. Pre-registration post, but fully registered practitioners may apply. Applications to Group Secretary. (7165)

BLACKBURN, QUEEN'S PARK HOSPITAL
1,020 General Beds)

SENIOR HOUSE OFFICER (Medicine)
required October 4, for acute medical unit. Apply to Secretary, H.M.C. Office, Royal Infirmary, Blackburn. (7164)

BRADFORD, ST. LUKE'S HOSPITAL
(828 beds)

SENIOR HOUSE OFFICER
(General Medicine and Clinical Pathology)
Vacant October 1. Applications, stating age, nationality, qualifications, and experience, with copy testimonials, to Secretary, Royal Infirmary, Bradford. (7325)

BURNLEY AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Burnley General Hospital (641 beds)

SENIOR HOUSE OFFICER (Medical)
The post offers good all-round experience under Consultant Staff. Applications, with two references, to Group Secretary, Burnley General Hospital. (7272)

LIVERPOOL, 14, BROADGREEN HOSPITAL

Applications are invited from registered medical practitioners for the appointment of
SENIOR HOUSE OFFICER (Medical)
to one of the two Medical Units at the hospital. The appointment is non-resident and the salary will be £765 per annum. Applications on forms obtainable from the undersigned should be returned completed not later than August 31, 1956.—H. Blythe, Group Secretary. (7285)

MERTHYR & ABERDARE HOSPITAL MANAGEMENT COMMITTEE

RESIDENT SENIOR HOUSE OFFICERS
(Medical)
St. Tydfil's Hospital, Merthyr Tydfil (376 beds)
Merthyr General Hospital, Merthyr Tydfil (120 beds)
Vacancy immediately for latter post, which terminates January 31, 1957. Apply with full particulars, and copies of two recent testimonials, to Group Secretary, St. Tydfil's Hospital, Merthyr Tydfil. (6884)

MOORGATE GENERAL HOSPITAL
(355 beds, 30 cots) and
BADSLEY MOOR LANE HOSPITAL, Rotherham
(70 beds)

SENIOR HOUSE OFFICER (Medicine)
required. Resident emoluments £150 per annum. Applications, with names of three referees, to Secretary, Hospital Management Committee, "Fern Bank," Doncaster Road, Rotherham. (6929)

NORTH & MID-CHESHIRE HOSPITAL MANAGEMENT COMMITTEE

Altrincham General Hospital and Annexe (130 beds)

SENIOR HOUSE OFFICER (Medical)
This appointment is in a busy hospital and offers excellent opportunities of practical experience. Post vacant end of September. Applications, together with two recent testimonials, to Group Secretary, The Hospital, Sinderland Road, Altrincham, Cheshire. (7203)

SCUNTHORPE HOSPITAL MANAGEMENT COMMITTEE

War Memorial Hospital, Scunthorpe (263 beds)

Applications are invited for
RESIDENT HOUSE PHYSICIANS
(a) SHO/Intern—vacant late September.
(b) Intern/SHO—vacant early October.
Busy department with medicine, paediatrics, skins and eyes, large out-patients clinics. Applications, naming two referees, to Group Secretary. (6903)

WESTCLIFF HOSPITAL, Balmoral Road, Westcliff-on-Sea, Essex

Applications are invited for the post of
RESIDENT MEDICAL OFFICER
(Senior House Officer Grade)
Post vacant September 1. The Hospital deals with communicable diseases and general medicine. The appointment covers a wide field of medicine and offers excellent training for general practice. Applications should be sent to the Secretary, General Hospital, Prittlewell Chase, Southend-on-Sea, Essex, as soon as possible. (7008)

WOKING VICTORIA HOSPITAL
Woking, Surrey (72 beds)

SENIOR HOUSE OFFICER
(post-registration appointment)
required for medical and surgical duties. Apply with two testimonials to Hospital Secretary. (6930)

BATTERSEA GENERAL HOSPITAL
Battersea Park, S.W.11

HOUSE PHYSICIAN
House Officer Grade. Resident, not Pre-registration. Apply Hospital Secretary, enclosing copies of two recent testimonials. (7122)

BOLINGBROKE HOSPITAL
Wandsworth Common, S.W.11

HOUSE PHYSICIAN (resident)
vacant September 15, 1956. Open to registered practitioners and pre-registration candidates. Apply Hospital Secretary, enclosing copies of three recent testimonials, by August 29, 1956. (6932)

LAMBETH HOSPITAL, Kennington, S.E.11

Applications are invited from pre-registration and registered medical practitioners for the position of
RESIDENT HOUSE PHYSICIAN
falling vacant on October 3, 1956. The successful applicant will be required to carry out a fortnight's locum duty starting on September 20, 1956. Application forms from the Physician Superintendent. A stamped addressed envelope should be enclosed. (6904)

MILE END HOSPITAL
Bancroft Road, London, E.1 (484 beds)

HOUSE PHYSICIAN (Pre- or Post-registration)
Post vacant September 22, 1956. Application forms obtainable from Physician Superintendent, should be returned by September 7, 1956, with copies of not more than three testimonials. (7334)

PRINCESS BEATRICE HOSPITAL
Earls Court, S.W.5

Applications are invited from Fully Registered Medical Practitioners for the post of
HOUSE PHYSICIAN
for 6 months (Junior House Officer Grade). Resident. Applications immediately, with three testimonials, to the House Governor. (7326)

CHELMSFORD, ST. JOHN'S HOSPITAL

HOUSE PHYSICIAN
(Pre-registration, 1st, 2nd, or 3rd appointment)
male or female, to commence September 24, 1956. Applications, stating age, nationality, qualifications and experience, together with recent testimonials, should be received not later than September 5, by the Secretary, Group Hospital Management Committee, Chelmsford and Essex Hospital, London Road, Chelmsford. (7166)

ROMFORD, ESSEX, VICTORIA HOSPITAL
(99 beds)

RESIDENT HOUSE PHYSICIAN (Male)
required early in September, 1956. (Post not approved for pre-registration purposes.) Applications should be forwarded to the Secretary, Romford Group H.M.C., Oldchurch Hospital, Romford (6644)

TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE

Middlesbrough General Hospital, Ayresome Green Lane, Middlesbrough (209 beds)

Applications are invited for the appointment of
HOUSE PHYSICIAN (Team No. 2)
at the above Hospital. Applications, stating age, experience and qualifications, together with names for reference, should be addressed to the Hospital Secretary. (6966)

HAMPSTEAD GENERAL HOSPITAL
Haverstock Hill, N.W.3
(Royal Free Hospital Group)

Applications are invited for the pre-registration post of
HOUSE PHYSICIAN
vacant October 1, 1956, tenable for a period of six months. Application forms may be obtained from the Secretary, to whom they should be returned, together with copies of three recent testimonials, by September 5, 1956. (Pr.7323)

NEW END HOSPITAL, London, N.W.3

Applications are invited for the post of
HOUSE PHYSICIAN (Gen. Med.)
Vacant October 1, 1956, preference will be given to Pre-registration candidate. Application forms from Group Secretary, 46, Cholmeley Park, N.6 (ARC. 3070 Ext. 24), and returnable to the Surgeon Superintendent, New End Hospital, by September 4, 1956. (Pr.7123)

ST. NICHOLAS HOSPITAL
Plumstead, S.E.18

HOUSE PHYSICIAN
Vacant October 3. Approved for pre-registration service. Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18. (Pr.7319)

BOURNEMOUTH & EAST DORSET HOSPITAL MANAGEMENT COMMITTEE

Royal Victoria Hospital, Shelley Road, Bournemouth

Applications are invited for the appointment of
TWO HOUSE PHYSICIANS
vacant September 18 and 20. The appointments are recognized for pre-registration purposes. Applications to the Hospital Secretary. (Pr.6887)

CAMBRIDGE, ADDENBROOKE'S HOSPITAL

HOUSE PHYSICIAN
for 6 months from October 17. Recognized pre-registration service. Apply, stating age, nationality, qualifications and experience (with dates), and copies of three testimonials, to Secretary by September 8. Interviews mid-September. (Pr.7145)

EAST SURREY HOSPITAL
Shrewsbury Road, Redhill

RESIDENT HOUSE PHYSICIAN
Pre-registration appointment, vacant late September. Apply Hospital Secretary, quoting two referees. (Pr.7146)

HIGH WYCOMBE & DISTRICT WAR MEMORIAL HOSPITAL
(160 beds)

PRE-REGISTRATION HOUSE PHYSICIAN
required for six months from September 15. Apply, with copies of two testimonials, to Group Secretary, St. Mary's Cottage, High Wycombe. (Pr.7147)

ILFORD AND BARKING GROUP HOSPITAL MANAGEMENT COMMITTEE

There will be a vacancy for a
HOUSE PHYSICIAN
at King George Hospital, Eastern Avenue, Ilford, on October 5, 1956. 1st or 2nd Post Pre-registration. The post will be tenable for six months. Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within seven days of the appearance of this advertisement.—H. F. Harris, Group Secretary. (Pr.7148)

Medicine—contd.

ROYAL HAMPSHIRE COUNTY HOSPITAL
Winchester (311 beds)

HOUSE PHYSICIAN (Pre-registration)
Vacant October 5, 1956. Applications, with copies of two testimonials, to the Secretary. (Pr.7249)

SEVENOAKS HOSPITAL, Sevenoaks, Kent

RESIDENT HOUSE PHYSICIAN (either sex)
Pre-registered post vacant September 26, 1956. Small busy General Hospital (81 beds) easily accessible to London and Coast. Apply Hospital Secretary. (Pr.7063)

TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE

North Ormesby Hospital (180 beds), Middlesbrough

Applications are invited for the appointment of
HOUSE PHYSICIAN
male or female, at the above-named Hospital. The appointment is recognized for pre-registration service under the Medical Act, 1950. Applications, stating full details, and giving two names for reference, should be addressed to the Hospital Secretary. (Pr.6934)

WEST BROMWICH AND DISTRICT GENERAL HOSPITAL (144 beds)

HOUSE PHYSICIAN
Vacant October 1, 1956. Pre-registration. Applications, with three recent testimonials, to Group Secretary, West Bromwich and District H.M.C., Edward Street, West Bromwich. (Pr.7384)

NEUROSURGERY

PRESTON AND CHORLEY HOSPITAL MANAGEMENT COMMITTEE

Manchester Regional Hospital Board
Preston Royal Infirmary (400 beds)

Applications are invited for the new appointment of
REGISTRAR IN THE DEPARTMENT OF NEURO-SURGERY
Preference will be given to candidates holding the F.R.C.S. This hospital is the neuro-surgical centre for the northern part of the Manchester Region. Application forms obtainable from the Group Secretary, Royal Infirmary, Preston. (6935)

BRISTOL, COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE

Frenchay Hospital (542 staffed beds—expanding)

Applications are invited for the post of
SENIOR HOUSE OFFICER
in the Regional Department of Neuro-Surgery. Vacant end of September. This post offers useful surgical experience and the opportunity of gaining a working knowledge of neurological diagnosis. Recognized for F.R.C.S. Two referees required. Applications to the Secretary, Frenchay Hospital, quoting "N.S.F." (7371)

OBSTETRICS AND GYNAECOLOGY

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

Wandsworth Hospital Group

REGISTRAR (Obstetrics & Gynaecology)
in Group Maternity Unit. Post vacant September 21. Recognized for M.R.C.O.G. Duties at St. James' Hospital and Weir Maternity Hospital. Application forms obtainable from Group Secretary, St. James' Hospital, Balham, S.W.12, to be completed and returned by September 8. (42738) (7283)

MANCHESTER REGIONAL HOSPITAL BOARD

Applications are invited for a resident post of
REGISTRAR
in the Obstetric and Gynaecology Department in the Barrow and Furness Group of Hospitals. The post will be available about November 1 next. 72 obstetric/gynaecological beds in main unit; outpatient departments and extensive surgical experience. Recognized for D.R.C.O.G. Applications to Group Secretary, Barrow and Furness Hospital Management Committee, 105, Abbey Road, Barrow-in-Furness, not later than September 6, 1956. (7251)

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

WHOLE-TIME GYNAECOLOGICAL AND OBSTETRICAL REGISTRAR
required at Edgware General and Bushey Maternity Hospitals. M.R.C.O.G. desirable. Department has 140 Obstetrical and 40 Gynaecological beds. Hospital may be visited by direct appointment. Application forms obtainable from, and returnable to, Group Secretary, Edgware General Hospital, Edgware, Middlesex, by September 4, 1956. (7363)

SHEFFIELD REGIONAL HOSPITAL BOARD

General Hospital, Boston (80 beds)

WHOLE-TIME RESIDENT REGISTRAR
(Obstetrics & Gynaecology)
required with relief duties in the Casualty Department. Appointment for one year in first instance. Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, by September 3, giving age, nationality, qualifications, present and previous appointments (with dates), naming three referees. (7157)

SOUTH CHESHIRE HOSPITAL MANAGEMENT COMMITTEE

REGISTRAR in Obstetrics and Gynaecology
(Resident)
Department of 60 beds. Considerable operative experience available. Main units at Nantwich and Crewe. Salary and conditions in accordance with Whitley Council regulations. Applications, stating age, qualifications, experience, and names of three referees, to Group Secretary, Group Headquarters, Barony Hospital, Nantwich. (7244)

CROYDON GROUP HOSPITAL MANAGEMENT COMMITTEE

Norwood Hospital

CLINICAL ASSISTANT, Gynaecology
1 Session weekly at £175 per annum. Detailed applications in writing, with names of two referees, to George A. Paines, Group Secretary, Croydon Hospital Management Committee, General Hospital, London Road, Croydon, within 7 days of the publication of this advertisement. (7204)

CAERNARVON AND ANGLESEY HOSPITAL MANAGEMENT COMMITTEE

St. David's Hospital, Bangor (136 beds and cots)
(Specialist Hospital for Obstetrics, Gynaecology and Paediatrics)
Part II Midwifery Training School

Applications are invited for the post of
RESIDENT SENIOR HOUSE OFFICER
in the Gynaecological and Obstetrical Department of the above Hospital. Previous gynaecological experience is essential. In the first instance the post will be in gynaecology—there will be opportunity for transfer to the obstetrical department at the end of six months. The post is recognized by the Royal College of Gynaecologists and Obstetricians for the Membership examination. Salary according to scale. Post vacant October 1, 1956. Applications, stating age, qualifications and experience, together with copies of three recent testimonials, to be forwarded to the Group Secretary, Plas Gwyn, Ffriddoedd Road, Bangor, within ten days of appearance of this advertisement. (7303)

DERBY CITY HOSPITAL

OBSTETRIC HOUSE SURGEON
(Pre-registration) or Senior House Officer
for duties at the Derby City Hospital (73 obstetric beds) and some duties at the Queen Mary Maternity Home (36 beds). Post vacant, September 25. Apply, stating age, qualifications and experience, with copies of two testimonials, to the Medical Superintendent. (7149)

HULL MATERNITY HOSPITAL (74 beds)

SENIOR HOUSE OFFICER (Obstetrics)
Applications are invited for the above resident appointment and tenable for one year. The post is recognized for the Diploma and the Membership of the Royal College of Obstetricians and Gynaecologists. This is the main Maternity Hospital for Hull and the East Riding of Yorkshire. The successful applicant will exercise general supervision over the three resident house surgeons. Applications stating age, qualifications and experience, with names and addresses of two referees, to the Hospital Secretary, Maternity Hospital, Hedon Road, Hull, as soon as possible. (7364)

KETTERING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Applications are invited for the post of
SENIOR HOUSE OFFICER
in Obstetrics and Gynaecology
commencing October 1, 1956, at St. Mary's Hospital, Kettering. Applications, giving particulars of qualifications and enclosing copies of three recent testimonials, to be sent to the Group Secretary, General Hospital, Kettering, Northants. (7330)

NOTTINGHAM CITY HOSPITAL (811 beds)

HOUSE OFFICER OBSTETRICS AND GYNAECOLOGY
(Recognized for pre-registration purposes)
Applications are invited for the above post, which will be graded Senior House Officer or House Officer in accordance with experience. Recognized for the M. and D.Obst.R.C.O.G. Post vacant on October 6, 1956. Applications, stating age, nationality, qualifications and experience, together with copies of not more than three testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall Road, Nottingham. (7049)

ST. HELENS & DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Whiston Hospital, Prescot (892 beds)
(Obstetrical Unit 73 beds)

SENIOR HOUSE OFFICER
Obstetrics and Gynaecology
Applications are invited for the above resident post, which is recognized for the M.R.C.O.G. and D.R.C.O.G. examinations. Previous obstetrical and gynaecological experience is essential. Applications, stating age, qualifications, experience and nationality, and giving two names for reference, should be forwarded to N. Richards, Group Secretary, Whiston Hospital, Prescot. (7286)

BARNET GENERAL HOSPITAL
Wellhouse Lane, Barnet, Herts

HOUSE SURGEON (Gynaecological)
required. Post vacant September 10. Apply to Hospital Secretary, giving details of experience, together with copies of two recent testimonials. (7118)

EDGWARE GENERAL HOSPITAL
Edgware, Middlesex

RESIDENT OBSTETRIC HOUSE SURGEON
Post vacant October 16, 1956. Six months' appointment. Post recognized for M.R.C.O.G. purposes. Applications, stating age, qualifications, experience and enclosing copies of up to three recent testimonials, to Medical Director of hospital by September 8, 1956. (7273)

EDGWARE GENERAL HOSPITAL
Edgware, Middlesex

RESIDENT GYNAECOLOGICAL HOUSE SURGEON
Post vacant October 11, 1956. Six months' appointment. Post recognized for M.R.C.O.G. purposes. Applications, stating age, qualifications, experience and enclosing copies of up to three recent testimonials, to Medical Director of hospital by September 8, 1956. (7274)

KENT AND CANTERBURY HOSPITAL
Canterbury (277 beds)

OBSTETRIC HOUSE SURGEON
The above post, which is recognized for the M.R.C.O.G. and D.Obst. becomes vacant in mid-September, 1956. N.H.S. salary and conditions. Applications, together with two recent testimonials, to be addressed to the Hospital Secretary at the above Hospital. (6775)

READING COMBINED HOSPITALS

Area Department of Obstetrics and Gynaecology
(104 beds)

Applications are invited from Registered Medical Practitioners, male and female, for the resident appointment of
GYNAECOLOGICAL HOUSE SURGEON
at the Royal Berkshire Hospital, Reading. Vacant October 1 and tenable for six months. Post recognized for M.R.C.O.G. Write, stating age and qualifications with dates, nationality and present appointment, with copy of one recent testimonial, to Secretary. (7316)

ROCHFORD, ESSEX, GENERAL HOSPITAL
(122 beds)

HOUSE OFFICER (Obstetrics)
required. Post vacant September 20, 1956. Recognized for D.Obst.R.C.O.G. The Hospital has 75 maternity beds, a Gynaecological Ward of 25 beds, and a Premature Baby Unit of 8 cots. Applications, stating age, etc., to the Secretary at the above Hospital by August 31, 1956.—J. C. Field, Secretary. (7009)

SUNDERLAND, ROYAL INFIRMARY (300 beds)

HOUSE OFFICER (male)
required for duties in Gynaecological & Urological Units. Post vacant September 26, 1956. Provisionally registered practitioners may apply. Applications, naming two referees, to the Hospital Secretary, Royal Infirmary, Sunderland. (7306)

HASTINGS AND ST. LEONARDS, BUCHANAN HOSPITAL (94 beds)

HOUSE SURGEON in Gynaecology
(29 Gynaecological beds). Post recognized for M.R.C.O.G., vacant September 22 for 6 months. Candidates for pre-registration service (Surgery) can be considered. Apply, giving names of three referees, to Hospital Administrator. (7181)

SOUTH SHIELDS MATERNITY HOSPITAL

HOUSE SURGEON
Obstetrics and Gynaecology
(Pre-registration, first or second post) required immediately, with duties at General Hospital (26 Gynaecological beds) and Maternity Hospital (36 Obstetrical beds). Applications to Medical Superintendent, General Hospital, South Shields. (Pr.7246)

OPHTHALMOLOGY

MID-KENT HOSPITAL MANAGEMENT COMMITTEE

Maidstone, Kent County Ophthalmic and Aural Hospital (113 beds)

Applications are invited for the appointment of
SENIOR HOUSE SURGEON
in the Ophthalmic Department of the above hospital. The hospital is recognized by the Examining Board for the F.R.C.S. and D.O. Salary £745 a year, less £150 a year for residential emoluments. Applications should be forwarded as soon as possible to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Church Street, Maidstone. (7338)

NORTH STAFFORDSHIRE ROYAL INFIRMARY (455 beds)

SENIOR HOUSE OFFICER (Ophthalmology) required. Recognized F.R.C.S. and D.O. Applications to Group Secretary, Hospital Management Committee, Princes Road, Stoke-on-Trent. (6905)

ROMFORD, ESSEX, OLDCHURCH HOSPITAL (722 beds)

SENIOR HOUSE OFFICER
required in the Department of Ophthalmology from September 8, 1956. Applications should be addressed immediately to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford. (7167)

ROYAL BUCKINGHAMSHIRE HOSPITAL Aylesbury, Bucks

HOUSE OFFICER, OPHTHALMOLOGY
required immediately. Post recognized for D.O. Apply with copies of two recent testimonials to Secretary-Superintendent as soon as possible. (6368)

ORTHOPAEDICS

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

SENIOR REGISTRAR
whole-time, non-resident, Orthopaedic and Traumatic Department, Central Middlesex Hospital, Park Royal, N.W.10. Duties include teaching and visiting convalescent hospital and area orthopaedic clinics. Opportunity of gaining at least 12 months' experience of long stay orthopaedic cases at Heatherwood Orthopaedic Hospital, Ascot. Applicants should be F.R.C.S. Post now vacant. Hospital may be visited by direct appointment. Application forms obtainable from and returnable to Secretary, Central Middlesex Group H.M.C., Park Royal, N.W.10, by September 8, 1956. (7350)

ALTON, HANTS, LORD MAYOR TRELOAR ORTHOPAEDIC HOSPITAL (340 beds)

Applications are invited from
SENIOR ORTHOPAEDIC REGISTRARS
who desire a year's experience in the same grade at a long-stay orthopaedic Hospital. Post includes attendance at peripheral clinics. Residence available. Write to Secretary for application form. (7257)

EAST ANGLIAN REGIONAL HOSPITAL BOARD

ORTHOPAEDIC REGISTRAR
Ipswich and East Suffolk Hospital. Post provides excellent training in orthopaedic surgery. Appointment for one year, renewable for second year. Applications, stating age, experience, and the names of three referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton Road, Cambridge, by September 3, 1956. Candidates invited to visit hospital by direct arrangement with H.M.C. Secretary at the hospital. (7205)

LEEDS REGIONAL HOSPITAL BOARD

REGISTRAR IN ORTHOPAEDIC SURGERY
St. James's Hospital, Leeds (64 Orthopaedic beds), and the Public Dispensary, Leeds. Non-resident. Applications, stating age, qualifications and details of present and previous appointments (showing dates), together with the names and addresses of three referees, to the Secretary, Joint Registrars Committee, Park Parade, Harrogate, by September 7, 1956. (7206)

LIVERPOOL REGIONAL HOSPITAL BOARD

Walton Hospital

Applications are invited for the post of
ORTHOPAEDIC REGISTRAR
with duties at the above hospital. Forms of application obtained from and to be returned to Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James Street, Liverpool, 2, to be received not later than September 8, 1956.—Vincent Collinge, Secretary to the Board. (7348)

SHEFFIELD REGIONAL HOSPITAL BOARD

Scunthorpe & District War Memorial Hospital (367 beds)
(Recognized for training for F.R.C.S.)

WHOLE-TIME RESIDENT REGISTRAR (Orthopaedics)
required. Appointment for one year in first instance. Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, by September 3, giving age, nationality, qualifications, present and previous appointments (with dates), naming three referees. (7151)

WELSH REGIONAL HOSPITAL BOARD

REGISTRAR (Orthopaedics)
Royal Gwent Hospital, Newport. Separate fracture and orthopaedic unit (36 beds). Own Out-patient, X-ray and Rehabilitation Departments. Non-resident. Subject to review end of first year. Application forms from S.A.M.O., Temple of Peace, Cathays Park, Cardiff, within 14 days. (7340)

WANDSWORTH HOSPITAL GROUP

St. James' Hospital, Balham, London, S.W.12

SENIOR HOUSE OFFICER (Orthopaedic and Trauma)
Post recognized for F.R.C.S. Vacant September 15. Applications, stating age, qualifications, experience and two referees, to Group Secretary at above address by September 5. (42740) (7313)

BIRMINGHAM, 15, ROYAL ORTHOPAEDIC HOSPITAL
Recognized by Royal College of Surgeons. 336 beds for long and short term orthopaedic cases (non-traumatic) and extensive out-patient services.

SENIOR HOUSE OFFICER
Registered Medical Practitioner preferably with orthopaedic experience. Residential charge £150 per annum. Applications, with testimonials, or names of referees, to Administrator. (7217)

CHERTSEY, SURREY, ST. PETER'S HOSPITAL (Late Botleys Park War Hospital) (430 beds)

ORTHOPAEDIC HOUSE SURGEON
required from August 28, 1956. 100 Orthopaedic beds. S.H.O. or H.O. (Intern grade). Post recognized for F.R.C.S. and Pre-registration service. Preference given to provisionally registered candidates. Salary in accordance with terms and conditions of National Health Service. Applications, together with names and addresses of referees, to be sent to the Physician Superintendent, St. Peter's Hospital, Chertsey, as soon as possible. (6304)

MARGATE, ROYAL SEA BATHING HOSPITAL (Surgical Tuberculosis and Orthopaedics) (341 beds)

SENIOR HOUSE OFFICER
The above post (one of two) is largely an orthopaedic one, and affords experience in the treatment of tuberculous and non-tuberculous orthopaedic conditions. There is also a genito-urinary unit of 35 beds and a small number of beds for other tuberculous conditions. The post is recognised for the F.R.C.S., and is suitable for someone reading for a higher surgical examination. Salary £745 per annum, less £150 for residential emoluments. Applications, with copies of testimonials, to Hospital Secretary. (5974)

MONTAGU HOSPITAL, MEXBOROUGH (168 beds)

SENIOR HOUSE OFFICER (Casualty and Orthopaedics)
£150 per annum residential emoluments. Recognized for training for F.R.C.S. Applications to the Secretary to the Committee, "Fern Bank," Doncaster Road, Rotherham. (7150)

NEWMARKET GENERAL HOSPITAL, Suffolk

Applications are invited for the post, now vacant, of
SENIOR HOUSE OFFICER
for Orthopaedic and Casualty duties. The post is resident and applications, giving age, nationality and qualifications, together with three recent testimonials, should be sent to the Medical Superintendent. (7115)

SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE

Salisbury General Hospital (Orthopaedic Department)

SENIOR HOUSE OFFICER (Resident) or RESIDENT HOUSE SURGEON
Applications are invited for the above post, which is also recognised for pre-registration candidates. The Department has over 50 beds and a large Out-patient turnover, dealing with fractures and all types of orthopaedic surgery. Applications, stating age, nationality, qualifications and experience, and naming two referees, to the Group Secretary, Odstock Hospital, Salisbury, as soon as possible. (6942)

SOUTHPORT PROMENADE HOSPITAL

SENIOR HOUSE OFFICER (resident)
Duties mainly connected with Orthopaedic and E.N.T. departments. Post vacant about mid-September. Apply stating age, experience, qualifications, nationality, and enclosing copies of two recent testimonials, to Group Secretary, Southport & District H.M.C., Promenade Hospital, Southport. (7287)

TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE

Pembury Hospital
Pembury, near Tunbridge Wells

Applications invited for appointment of
HOUSE SURGEON (Senior House Officer)
to Orthopaedic Unit. Post vacant September 1, 1956, recognized for F.R.C.S. (Eng.) and tenable for one year. Work includes treatment of long and short stay cases and traumatic surgery with large Out-patient and Fracture Clinics. National Health Service Salary, less £150 per annum for board, lodging, etc. Accommodation for a married man could be arranged. Apply stating age, qualifications and experience with three testimonials, to Group Secretary, Sherwood Park, Pembury Road, Tunbridge Wells. (7331)

ST. NICHOLAS HOSPITAL Plumstead, S.E.18

HOUSE OFFICER
(Orthopaedic, Fracture & Casualty Departments)
Vacant now. Recognized for F.R.C.S. 6 months' resident post-registration appointment providing good general experience in a busy acute general hospital. Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18. (7116)

BEVERLEY, YORKSHIRE, WESTWOOD HOSPITAL (229 beds)

ORTHOPAEDIC HOUSE SURGEON
(1st, 2nd or 3rd post)
Married accommodation available. Offers good opportunity for general experience in busy acute general hospital. Approved pre-registration post. Fully registered practitioners may apply. Recognized for F.R.C.S. Vacant now. Apply Group Secretary. (6943)

BLACK NOTLEY HOSPITAL Braintree, Essex (516 beds)

Applications invited for post of
HOUSE OFFICER (Orthopaedic Surgery)
Duties include care of cases from London Hospital Orthopaedic Department. First, second, third or pre-registration post: tenable for 6 months. Recognized for F.R.C.S. Applications, with copies of three testimonials, to Group Secretary, Colchester H.M.C., 14, Pope's Lane, Colchester, Essex. (7275)

NORTHAMPTON GENERAL HOSPITAL (482 beds)

Vacancy October 1, 1956, for
FRACTURE AND ORTHOPAEDIC HOUSE OFFICER
Recognized for F.R.C.S. and for pre-registration. Six months' appointment in first instance. Applications, as soon as possible, to S. G. Hill, Superintendent. (Pr.7152)

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE

Royal Portsmouth Hospital

HOUSE OFFICER (pre-registration)
Orthopaedic Department, 104 beds. Vacant now. Applications, stating age, experience and qualifications, together with the names of two referees, should be forwarded as soon as possible to E. H. Hurst, 35, Grove Road South, Southsea. (Pr.6371)

SOUTHAMPTON, ROYAL SOUTH HANTS HOSPITAL (278 beds)

ORTHOPAEDIC HOUSE SURGEON
required. Post recognized for pre-registration service and tenable for 6 months. The Hospital is the centre to which all trauma from a large industrial town and port is directed, thus providing excellent experience in the treatment of traumatic conditions; patients with orthopaedic conditions are also drawn from a wide area. Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar Street, Southampton. (Pr.6442)

PAEDIATRICS

HAMMERSMITH HOSPITAL & INSTITUTES OF OBSTETRICS AND CHILD HEALTH
Du Cane Road, London, W.12

RESIDENT PAEDIATRIC REGISTRAR
required. Post vacant October 23. Duties involve care of new-born babies in Maternity Department and Premature Baby Unit. Age, qualifications, experience, names two referees, to Secretary, Board of Governors, by September 8. (7292)

Paediatrics—contd.

LANCASTER, BEAUMONT HOSPITAL, Slyne Road

PAEDIATRIC REGISTRAR (Resident)

Previous Paediatric experience essential. Duties include experience in Children's Medical Ward, in Neonatal unit, and Paediatric out-patient clinics. Unit recognized for D.C.H. Candidates may visit hospital by direct appointment. Application, together with names of two referees, to Group Secretary, Royal Lancaster Infirmary, Lancaster. (7302)

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

REGISTRAR

required at Cell Barnes Hospital, St. Albans, Herts. This is a modern hospital where 895 mentally defective persons of all types, including children, are under care. Approved for D.P.M. Hospital may be visited by direct appointment. Application forms obtainable from, and returnable to, Group Secretary, Hospital Management Committee, Harperbury Hospital, St. Albans, Herts, by September 10, 1956. (7351)

OXFORD REGIONAL HOSPITAL BOARD

REGISTRAR IN PAEDIATRICS

to hospitals of the Northampton and Kettering area with duties mainly at Northampton General Hospital. Applicants holding or wishing to take the D.C.H. preferred. Post provides general experience in Paediatrics and includes specific fevers and neo-natal work. The appointment will be for one year and eligible for extension to two years. Applications on forms obtainable from the Secretary, Registrars Committee, 43, Banbury Road, Oxford, should reach him by September 14, 1956. (7207)

SHEFFIELD REGIONAL HOSPITAL BOARD

Lincoln County Hospital (200 beds)

WHOLE-TIME RESIDENT REGISTRAR (Paediatrics)

required. Appointment for one year in first instance. Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, by September 3, giving age, nationality, qualifications, present and previous appointments (with dates), naming three referees. (7153)

CARSHALTON, SURREY, QUEEN MARY'S HOSPITAL FOR CHILDREN (General Children's Hospital of 853 beds)

SENIOR HOUSE OFFICERS

Two required, care of acute medical, rheumatism and poliomyelitis beds. Applications, stating age, qualifications and experience, with copies of three testimonials, should reach the Group Secretary, by September 1, 1956. (7168)

HEREFORD COUNTY HOSPITAL

SENIOR HOUSE OFFICER (Paediatrics)

required October 5, 1956, for unit of 60 beds. Applications in writing, together with names of two referees, to Group Secretary, Victoria House, Elgin Street, Hereford. (7290)

IPSWICH & EAST SUFFOLK HOSPITAL Heath Road Wing, Ipswich (274 beds)

Applications invited for the post of

SENIOR HOUSE OFFICER (resident)

to the Paediatric Unit, vacant on September 29. Recognized for D.C.H., and normally of 12 months' tenure. Detailed applications, with copies of two recent testimonials, to the Hospital Secretary. (6891)

SOUTH MANCHESTER H.M.C.

The Duchess of York Hospital for Babies and Wythenshawe Hospital

Applications are invited for the post of

SENIOR HOUSE OFFICER

vacant October 1. A joint post of not less than 3 months and preferably 6 months at each Hospital is recognized as training for the D.C.H. The Duchess of York Hospital is also attached to the Manchester University Department of Child Health. Applications to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of the appearance of this advertisement. (7076)

CHELMSFORD, ST. JOHN'S HOSPITAL

Applications are invited from registered practitioners for the post of

RESIDENT PAEDIATRIC HOUSE OFFICER (male or female)

Commencing September 15, 1956, to work in the Paediatric Unit of the Chelmsford Hospital Group. The Unit includes a Premature Baby Nursery of 10 cots and a Neo-natal Department in the Maternity Block of the Hospital. The Department is recognized for the D.C.H. Applications, stating age, nationality, qualifications and experience, together with recent testimonials, should be received not later than August 28, 1956, by the Group Secretary, Chelmsford Group Hospital Management Committee, Chelmsford and Essex Hospital, London Road, Chelmsford. (6968)

HULL (A) GROUP HOSPITAL MANAGEMENT COMMITTEE

HOUSE PHYSICIAN—Paediatric Unit

Duties at Victoria Children's Hospital for three months, followed by three months on the paediatric wards, Western General Hospital. An interesting and varied post which includes out-patient and casualty work. This appointment, which commences on October 1, 1956, is recognized for the D.C.H. Apply, giving experience, testimonials, etc., to the Secretary, Western General Hospital, Anlaby Road, Hull. (6668)

HULL (A) GROUP HOSPITAL MANAGEMENT COMMITTEE

Victoria Hospital for Sick Children, Park Street, Hull

HOUSE SURGEON

required for the above hospital. Registration or pre-registration post. Six monthly term. Recognized for the D.C.H. qualification. Salary according to National Scales. Replies, with testimonials, should be sent to the Hospital Secretary. (7245)

KENT AND CANTERBURY HOSPITAL Canterbury (277 beds)

PAEDIATRIC HOUSE PHYSICIAN

The above post, recognized for D.C.H., includes work in the Ward and Out-patient Department and also provides experience in the care of the new-born. Opportunities exist for the study of preventive medicine among children and child guidance work. Post vacant at the end of September, 1956. N.H.S. salary and conditions. Applications, together with two testimonials, to be addressed to the Hospital Secretary at the above Hospital. (6776)

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Royal Berkshire Hospital (399 beds), Reading

Applications are invited from registered and provisionally registered medical practitioners for the resident post of

HOUSE PHYSICIAN

in the Paediatric Department; vacant September 15 for six months. Write, before September 3, stating age, qualifications with dates, nationality, present post, with one copy of recent testimonial, to Secretary. (6813)

NORTHAMPTON GENERAL HOSPITAL (483 beds)

Vacancy October 1, 1956, for

PAEDIATRIC HOUSE OFFICER

Post recognized for D.C.H. and for pre-registration. Six months' appointment in first instance. Person appointed will be required to reside alternately with another Paediatric House Officer, for three month periods at Northampton General Hospital and Harborough Road Hospital, Northampton, and whilst at the latter hospital to be responsible to the Consultants (or the supervision of all the beds, allocated as follows: Sub-acute Paediatric 20, Dermatological 16, General Medical 30, Infectious Diseases 46 (mostly children but including polios). Applications as soon as possible to S. G. Hill, Superintendent. (Pr.7156)

STOKE-ON-TRENT, CITY GENERAL HOSPITAL

HOUSE OFFICER (Paediatrics)

required, vacant very shortly. Pre-registration post. Detailed applications, with copy testimonials, to Group Secretary, Princes Road, Stoke-on-Trent. (Pr.7168)

PATHOLOGY

SHEFFIELD REGIONAL HOSPITAL BOARD

WHOLE-TIME CONSULTANT PATHOLOGIST

required, based on Grimsby General Hospital. Duties will involve responsibility for public health and hospital bacteriology for the Grimsby area and considerable experience in these is essential. Some experience of morbid anatomy will also be required. Appointment to commence in January, 1957. Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, 10. Forms to be returned by September 22. (7218)

SHEFFIELD REGIONAL HOSPITAL BOARD

WHOLE-TIME CONSULTANT PATHOLOGIST

required, based on Scunthorpe and District War Memorial Hospital. Appointee to commence on or after January 1, 1957. Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, 10. Forms to be returned by September 22. (7219)

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN Clapham Common, S.W.4

REGISTRAR IN PATHOLOGY

(Full-time). Applications are invited from women medical practitioners who should have had experience of laboratory work. Canvassing will disqualify, but candidates are not precluded from visiting the hospital if they so desire. Forms of application (enclosing stamped addressed envelope) from the Secretary, Lambeth Group Hospital Management Committee, Renfrew Road, S.E.11, to whom completed applications should be returned not later than September 15, 1956. (7170)

MANCHESTER REGIONAL HOSPITAL BOARD AND THE BOARD OF GOVERNORS OF THE UNITED MANCHESTER HOSPITALS

SENIOR REGISTRAR IN PATHOLOGY

Facilities for training in all branches of pathology will be provided in both teaching and non-teaching hospitals in the Manchester area. Main duties initially at Manchester Royal Infirmary. Application forms, obtainable from the Senior Administrative Medical Officer, Manchester Regional Hospital Board, Chestwood Road, Manchester, 8, should be returned by September 3, 1956. (7315)

UNITED OXFORD HOSPITALS

Applications invited for the post of non-resident

REGISTRAR in the Department of Pathology

Radcliffe Infirmary, from October 19, 1956. Applications, on forms obtainable from the Administrator, Radcliffe Infirmary, Oxford, should be received not later than September 10, 1956. (7154)

NORTHAMPTON GENERAL HOSPITAL (483 beds)

Vacancy October 1, 1956, for

SENIOR HOUSE OFFICER

in Department of Pathology. Appointment to March 31, 1957, in first instance, and afterwards by agreement. Applications, with names of three referees, as soon as possible to S. G. Hill, Superintendent. (7155)

IMPORTANT: All intending applicants should read the revised NOTICE at the top of page 28

MEDICAL INSURANCE AGENCY LTD.
Chairman: James Fenton, CBE, MD. General Manager: A. N. Dixon, ACII. Hon. Secretary: Henry Robinson, MD, DL, JP.
B.M.A. HOUSE, TAVISTOCK SQ., LONDON, W.C.1
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FAMILY PROVISION
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OPHTHALMOLOGY

MID-KENT HOSPITAL MANAGEMENT COMMITTEE

Maidstone, Kent County Ophthalmic and Aural Hospital (113 beds)

Applications are invited for the appointment of
SENIOR HOUSE SURGEON
in the Ophthalmic Department of the above hospital. The hospital is recognised by the Examining Board for the F.R.C.S. and D.O. Salary £745 a year, less £150 a year for residential emoluments. Applications should be forwarded as soon as possible to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Church Street, Maidstone. (7338)

NORTH STAFFORDSHIRE ROYAL INFIRMARY (453 beds)

SENIOR HOUSE OFFICER (Ophthalmology) required. Recognised F.R.C.S. and D.O. Applications to Group Secretary, Hospital Management Committee, Princes Road, Stoke-on-Trent. (6905)

ROMFORD, ESSEX, OLDCHURCH HOSPITAL (722 Beds)

SENIOR HOUSE OFFICER
required in the Department of Ophthalmology from September 6, 1956. Applications should be addressed immediately to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford. (7167)

ROYAL BUCKINGHAMSHIRE HOSPITAL Aylesbury, Bucks

HOUSE OFFICER, OPHTHALMOLOGY required immediately. Post recognized for D.O. Apply with copies of two recent testimonials to Secretary-Superintendent as soon as possible. (6368)

ORTHOPAEDICS

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

SENIOR REGISTRAR
whole-time, non-resident, Orthopaedic and Traumatic Department, Central Middlesex Hospital, Park Royal, N.W.10. Duties include teaching and visiting convalescent hospital and area orthopaedic clinics. Opportunity of gaining at least 12 months' experience of long stay orthopaedic cases at Heatherwood Orthopaedic Hospital, Ascot. Applicants should be F.R.C.S. Post now vacant. Hospital may be visited by direct appointment. Application forms obtainable from and returnable to Secretary, Central Middlesex Group H.M.C., Park Royal, N.W.10, by September 8, 1956. (7350)

ALTON, HANTS, LORD MAYOR TRELOAR ORTHOPAEDIC HOSPITAL (340 beds)

Applications are invited from
SENIOR ORTHOPAEDIC REGISTRARS
who desire a year's experience in the same grade in a long-stay orthopaedic Hospital. Post includes attendance at peripheral clinics. Residence available. Write to Secretary for application form. (7257)

EAST ANGLIAN REGIONAL HOSPITAL BOARD

ORTHOPAEDIC REGISTRAR
Ipswich and East Suffolk Hospital. Post provides excellent training in orthopaedic surgery. Appointment for one year, renewable for second year. Applications, stating age, experience, and the names of three referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton Road, Cambridge, by September 3, 1956. Candidates invited to visit hospital by direct arrangement with H.M.C. Secretary at the hospital. (7205)

LEEDS REGIONAL HOSPITAL BOARD

REGISTRAR IN ORTHOPAEDIC SURGERY
St. James's Hospital, Leeds (64 Orthopaedic beds), and the Public Dispensary, Leeds. Non-resident. Applications, stating age, qualifications and details of present and previous appointments (showing dates), together with the names and addresses of three referees, to the Secretary, Joint Registrars Committee, Park Parade, Harrogate, by September 7, 1956. (7206)

LIVERPOOL REGIONAL HOSPITAL BOARD

Walton Hospital

Applications are invited for the post of
ORTHOPAEDIC REGISTRAR
with duties at the above hospital. Forms of application obtained from and to be returned to Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James Street, Liverpool, 2, to be received not later than September 8, 1956.—Vincent Cottinge, Secretary to the Board. (7318)

SHEFFIELD REGIONAL HOSPITAL BOARD

Scunthorpe & District War Memorial Hospital (247 beds)
(Recognized for training for F.R.C.S.)

WHOLE-TIME RESIDENT REGISTRAR (Orthopaedics)
required. Appointment for one year in first instance. Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, by September 3, giving age, nationality, qualifications, present and previous appointments (with dates), naming three referees. (7151)

WELSH REGIONAL HOSPITAL BOARD

REGISTRAR (Orthopaedics)
Royal Gwent Hospital, Newport. Separate fracture and orthopaedic unit (36 beds). Own Out-patient, X-ray and Rehabilitation Departments. Non-resident. Subject to review end of first year. Application forms from S.A.M.O., Temple of Peace, Cathays Park, Cardiff, within 14 days. (7340)

WANDSWORTH HOSPITAL GROUP

St. James' Hospital, Balham, London, S.W.12

SENIOR HOUSE OFFICER (Orthopaedic and Trauma)
Post recognized for F.R.C.S. Vacant September 15. Applications, stating age, qualifications, experience and two referees, to Group Secretary at above address by September 5. (427/40) (7313)

BIRMINGHAM, 15. ROYAL ORTHOPAEDIC HOSPITAL
Recognized by Royal College of Surgeons. 336 beds for long and short term orthopaedic cases (non-traumatic) and extensive out-patient services.

SENIOR HOUSE OFFICER
Registered Medical Practitioner preferably with orthopaedic experience. Residential charge £150 per annum. Applications, with testimonials, or names of referees, to Administrator. (7217)

CHERTSEY, SURREY, ST. PETER'S HOSPITAL (Late Botleys Park War Hospital) (430 beds)

ORTHOPAEDIC HOUSE SURGEON
required from August 28, 1956. 100 Orthopaedic beds. S.H.O. or H.O. (Intern grade). Post recognized for F.R.C.S. and Pre-registration service. Preference given to provisionally registered candidates. Salary in accordance with terms and conditions of National Health Service. Applications, together with names and addresses of referees, to be sent to the Physician Superintendent, St. Peter's Hospital, Chertsey, as soon as possible. (6304)

MARGATE, ROYAL SEA BATHING HOSPITAL (Surgical Tuberculosis and Orthopaedics) (341 beds)

SENIOR HOUSE OFFICER
The above post (one of two) is largely an orthopaedic one, and affords experience in the treatment of tuberculous and non-tuberculous orthopaedic conditions. There is also a genito-urinary unit of 35 beds and a small number of beds for other tuberculous conditions. The post is recognized for the F.R.C.S., and is suitable for someone reading for a higher surgical examination. Salary £745 per annum, less £150 for residential emoluments. Applications, with copies of testimonials, to Hospital Secretary. (5974)

MONTAGU HOSPITAL, MEXBOROUGH (168 beds)

SENIOR HOUSE OFFICER (Casualty and Orthopaedics)
£150 per annum residential emoluments. Recognized for training for F.R.C.S. Applications to the Secretary to the Committee, "Fern Bank," Doncaster Road, Rotherham. (7150)

NEWMARKET GENERAL HOSPITAL, Suffolk

Applications are invited for the post, now vacant, of
SENIOR HOUSE OFFICER
for Orthopaedic and Casualty duties. The post is resident and applications, giving age, nationality and qualifications, together with three recent testimonials, should be sent to the Medical Superintendent. (7115)

SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE

Salisbury General Hospital (Orthopaedic Department)

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Duties mainly connected with Orthopaedic and E.N.T. departments. Post vacant about mid-September. Apply stating age, experience, qualifications, nationality, and enclosing copies of two recent testimonials, to Group Secretary, Southport & District H.M.C., Promenade Hospital, Southport. (7287)

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Pembury, near Tunbridge Wells

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Du Cane Road, London, W.12

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Paediatrics—contd.

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Previous Paediatric experience essential. Duties include experience in Children's Medical Ward, in Neonatal unit, and Paediatric out-patient clinics. Unit recognized for D.C.H. Candidates may visit hospital by direct appointment. Applications, together with names of two referees, to Group Secretary, Royal Lancaster Infirmary, Lancaster. (7302)

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(General Children's Hospital of 853 beds)

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SOUTH MANCHESTER H.M.C.

The Duchess of York Hospital for Babies and Wythenshawe Hospital

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vacant October 1. A joint post of not less than 3 months and preferably 6 months at each Hospital is recognized as training for the D.C.H. The Duchess of York Hospital is also attached to the Manchester University Department of Child Health. Applications to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of the appearance of this advertisement. (7076)

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HULL (A) GROUP HOSPITAL MANAGEMENT COMMITTEE

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Duties at Victoria Children's Hospital for three months, followed by three months on the paediatric wards, Western General Hospital. An interesting and varied post which includes out-patient and casualty work. This appointment, which commences on October 1, 1956, is recognized for the D.C.H. Apply, giving experience, testimonials, etc., to the Secretary, Western General Hospital, Anlaby Road, Hull. (6660)

HULL (A) GROUP HOSPITAL MANAGEMENT COMMITTEE

Victoria Hospital for Sick Children, Park Street, Hull

HOUSE SURGEON

required for the above hospital. Registration or pre-registration post. Six monthly term. Recognized for the D.C.H. qualification. Salary according to National Scales. Replies, with testimonials, should be sent to the Hospital Secretary. (7245)

KENT AND CANTERBURY HOSPITAL
Canterbury (277 beds)

PAEDIATRIC HOUSE PHYSICIAN

The above post, recognized for D.C.H., includes work in the Ward and Out-patient Department and also provides experience in the care of the new-born. Opportunities exist for the study of preventive medicine among children and child guidance work. Post vacant at the end of September, 1956. N.H.S. salary and conditions. Applications, together with two testimonials, to be addressed to the Hospital Secretary at the above Hospital. (6776)

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Royal Berkshire Hospital (399 beds), Reading

Applications are invited from registered and provisionally registered medical practitioners for the resident post of
HOUSE PHYSICIAN
in the Paediatric Department; vacant September 15 for six months. Write, before September 3, stating age, qualifications with dates, nationality, present post, with one copy of recent testimonial, to Secretary. (6813)

NORTHAMPTON GENERAL HOSPITAL
(483 beds)

Vacancy October 1, 1956, for
PAEDIATRIC HOUSE OFFICER
Post recognized for D.C.H. and for pre-registration. Six months' appointment in first instance. Person appointed will be required to reside alternately with another Paediatric House Officer, for three month periods at Northampton General Hospital and Harborough Road Hospital, Northampton, and whilst at the latter hospital to be responsible to the Consultants for the supervision of all the beds, allocated as follows: Sub-acute Paediatric 20, Dermatological 16, General Medical 30, Infectious Diseases 46 (mostly children but including polios). Applications as soon as possible to S. G. Hill, Superintendent. (Pr.7156)

STOKE-ON-TRENT, CITY GENERAL HOSPITAL

HOUSE OFFICER (Paediatrics)

required, vacant very shortly. Pre-registration post. Detailed applications, with copy testimonials, to Group Secretary, Princes Road, Stoke-on-Trent. (Pr.7169)

PATHOLOGY

SHEFFIELD REGIONAL HOSPITAL BOARD

WHOLE-TIME CONSULTANT PATHOLOGIST

required, based on Grimsby General Hospital. Duties will involve responsibility for public health and hospital bacteriology for the Grimsby area and considerable experience in these is essential. Some experience of morbid anatomy will also be required. Appointment to commence in January, 1957. Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, 10. Forms to be returned by September 22. (7218)

SHEFFIELD REGIONAL HOSPITAL BOARD

WHOLE-TIME CONSULTANT PATHOLOGIST

required, based on Scunthorpe and District War Memorial Hospital. Appointee to commence on or after January 1, 1957. Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, 10. Forms to be returned by September 22. (7219)

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN
Clapham Common, S.W.4

REGISTRAR IN PATHOLOGY

(Full-time). Applications are invited from women medical practitioners who should have had experience of laboratory work. Canvassing will disqualify, but candidates are not precluded from visiting the hospital if they so desire. Forms of application (enclosing stamped addressed envelope) from the Secretary, Lambeth Group Hospital Management Committee, Renfrew Road, S.E.11, to whom completed applications should be returned not later than September 15, 1956. (7170)

MANCHESTER REGIONAL HOSPITAL BOARD AND THE BOARD OF GOVERNORS OF THE UNITED MANCHESTER HOSPITALS

SENIOR REGISTRAR IN PATHOLOGY

Facilities for training in all branches of pathology will be provided in both teaching and non-teaching hospitals in the Manchester area. Main duties initially at Manchester Royal Infirmary. Application forms, obtainable from the Senior Administrative Medical Officer, Manchester Regional Hospital Board, Cheetwood Road, Manchester, 8, should be returned by September 3, 1956. (7319)

UNITED OXFORD HOSPITALS

Applications invited for the post of non-resident
REGISTRAR in the Department of Pathology
Radcliffe Infirmary, from October 19, 1956. Applications, on forms obtainable from the Administrator, Radcliffe Infirmary, Oxford, should be received not later than September 10, 1956. (7154)

NORTHAMPTON GENERAL HOSPITAL
(483 beds)

Vacancy October 1, 1956, for
SENIOR HOUSE OFFICER
in Department of Pathology. Appointment to March 31, 1957, in first instance, and afterwards by agreement. Applications, with names of three referees, as soon as possible to S. G. Hill, Superintendent. (7155)

IMPORTANT: All intending applicants should read the revised NOTICE at the top of page 28

MEDICAL INSURANCE AGENCY LTD.
Chairman: James Fenton, CBE, MD. General Manager: A. N. Dixon, ACII. Hon. Secretary: Henry Robinson, MD, DL, JP.
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PHYSICAL MEDICINE

ST. THOMAS' HOSPITAL, London, S.E.1

SENIOR REGISTRAR
in the Department of Physical Medicine

For a period of one year in the first instance. Applications, naming two referees, to the Clerk of the Governors by September 7, 1956. (7101)

BELFAST HOSPITAL MANAGEMENT COMMITTEE
Riddel House, Royal Victoria Hospital, Belfast

SENIOR HOUSE OFFICER

Applications are invited from candidates training for Part II, Diploma of Physical Medicine. Salary £745 per annum. Application to be made on a form obtainable from the Secretary, Belfast Hospital Management Committee, Riddel House, Royal Victoria Hospital, Belfast, not later than September 3, 1956. (7304)

PLASTIC SURGERY

PLASTIC SURGERY, JAW INJURIES AND BURNS CENTRE
St. Lawrence Hospital, Chepstow, Mon.
(127 Plastic Surgery, 50 Orthopaedic Beds)

SENIOR HOUSE OFFICER
in Plastic Surgery

required. Previous experience in Specialty not essential. The hospital intakes from most of Wales and the successful candidate will receive a thorough training. There is a second S.H.O. in Plastic Surgery and also a S.H.O. in Orthopaedics, Senior Registrar non-resident, and two Registrars, all in plastic Surgery resident. Salary £745, less £150 board residence. Write, quoting two referees, to T. A. Jones, Group Secretary, 64, Cardiff Road, Newport, Mon. (7158)

PSYCHIATRY

SOUTH WESTERN REGIONAL HOSPITAL BOARD

St. Lawrence's Hospital, Bodmin, and Horton Road and Coney Hill Hospitals, Gloucester

Applications are invited for two whole-time appointments of

CONSULTANT PSYCHIATRIST

one to the West Cornwall Clinical Area with duties mainly at St. Lawrence's Hospital, Bodmin, and the other to the North Gloucestershire Clinical Area with duties mainly at Horton Road and Coney Hill Hospitals, Gloucester. Applicants must possess a higher qualification. Facilities for Out-patients'' clinic work exist in the North Gloucestershire Clinical Area. Residential accommodation is available for a married man at St. Lawrence's Hospital. Twelve copies of applications, stating date of birth, qualifications and experience, together with names and addresses of two referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park Road, Bristol, 8, not later than September 15, 1956. (7286)

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

WHOLE-TIME CONSULTANT PSYCHIATRIST

required at West Park Hospital, Epsom, Surrey. Candidates should possess D.P.M. and a higher medical qualification, and have wide knowledge of both psychiatry and general medicine. Applications, by letter (5 copies), giving date of birth, qualifications, experience, three referees, to Secretary (S.1), S.W. Met. R.H.B., 11a, Portland Place, W.1, by September 22, 1956. Applicants may visit hospital by local arrangement. (7220)

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

WHOLE-TIME CONSULTANT PSYCHIATRIST

required at Horton Hospital, Epsom, Surrey, a large mental hospital of 1,635 beds, of which 1,550 are at present occupied and which provides all modern methods of psychiatric treatment. Out-patient clinics are operated at certain London hospitals. Candidates should possess D.P.M. and preferably a higher medical qualification and have wide experience of psychiatry in all its branches. Residential accommodation is available at present for single persons only. Applications by letter (5 copies), giving date of birth, qualifications, experience, three referees, to Secretary (S.1), S.W. Met. R.H.B., 11a, Portland Place, W.1, by September 22, 1956. Applicants may visit hospital by local arrangement. (7221)

WELSH REGIONAL HOSPITAL BOARD

WHOLE-TIME CONSULTANT PSYCHIATRIST

Pen-y-Val Hospital and Maindiff Court Emrys Treatment Unit, Abergavenny (1,336 beds). Applicants must have had wide experience in Psychiatry, hold a Diploma in Psychological Medicine, be competent to take clinical responsibility and to participate in the work of the associated out-patient clinics and domiciliary consultant service in the area served by the hospital. Non-resident. Twelve copies of application, naming three referees, to S.A.M.O., Temple of Peace, Cathays Park, Cardiff, within 21 days. (7370)

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

WHOLE-TIME ASSISTANT PSYCHIATRIST (S.H.M.O. grade)

required to work at The Old Manor Hospital, Salisbury, under the direction of the Physician Superintendent of the Knowle Group. Candidates should possess D.P.M. and have experience of both in-patient and out-patient work in psychiatry. There is a house available at a reasonable rental. Applications by letter (5 copies) giving date of birth, qualifications, experience, three referees, to the Secretary (S.1), S.W. Met. R.H.B., 11, Portland Place, W.1, by September 22, 1956. Applicants may visit hospital by local arrangement. (7222)

BIRMINGHAM REGIONAL HOSPITAL BOARD

1. South Warwickshire Group 14, 50, Holly Walk, Leamington Spa
REGISTRAR, PSYCHIATRY

for Coventry, Nuneaton and Rugby Hospitals. Out-patients (adults and children). (7 sessions); 4 in-patients sessions at Central Hospital near Warwick with Neurosis Unit, E.E.G. Department, Occupational Therapy and all modern treatments. House or flat at Central Hospital.

2. Shrewsbury Group 15, Royal Salop Infirmary, Shrewsbury
REGISTRAR, PSYCHIATRY

at Shelton Mental Hospital. Whole-time. Previous experience general medicine desirable. Application forms from Group Secretaries to be returned by September 3, 1956. Candidates may visit Hospitals. (7208)

CHICHESTER, GRAYLINGWELL HOSPITAL

REGISTRAR (Lady or Gentleman)

required at the above Psychiatric Hospital which has Departments of Research and Neurology and to which are attached three active out-patients clinics. All modern treatments are practised and organized training is given for D.P.M. Furnished accommodation available for single officer. Candidates may visit the Hospital by arrangement with the Medical Superintendent. Application forms (obtainable from the Group Secretary) are returnable within 14 days of the appearance of this advertisement. (7246)

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE

Fairfield General Hospital

Applications are invited for the post of
JUNIOR HOSPITAL MEDICAL OFFICER
(Psychiatry)

The appointment is for one year in the first instance, subject to renewal annually. This post is recognized for the D.P.M. for twelve months. Applications, with full details of age, qualifications and experience, together with names of two referees, should be submitted to H. Wilkinson, Group Secretary, Bury General Hospital, Bury. (7252)

RADIOLOGY

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

PART-TIME CONSULTANT RADIOLOGIST
(3 h.d.p.w.)

required for the St. Helier (Surrey) Group. Candidates must have D.M.R. and wide experience in radiology. Applications by letter (5 copies) giving date of birth, qualifications, experience, three referees, to Secretary (S.1), S.W. Met. R.H.B., 11a, Portland Place, W.1, by September 22, 1956. Applicants may visit hospitals by local arrangement. (7124)

SHEFFIELD REGIONAL HOSPITAL BOARD

WHOLE-TIME ASSISTANT RADIOLOGIST

for Derbyshire Royal Infirmary to work under the direction of the Consultant Radiologist-in-charge. Candidates should possess a diploma in Radiology. Salary scale £1,575 by £50 to £2,025. Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, 10. Forms to be returned by September 15, 1956 (6974)

HAMMERSMITH HOSPITAL & POSTGRADUATE MEDICAL SCHOOL
Du Cane Road, London, W.12

WHOLE-TIME NON-RESIDENT REGISTRAR
(Radiodiagnostic)

required October 1. Age, qualifications, experience, names two referees, to Secretary, Board of Governors, by September 8. (7293)

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

REGISTRAR IN RADIOLOGY

X-ray Diagnostic Department, required at Royal Northern Hospital. Candidates should possess D.M.R.D. Hospital may be visited by direct appointment. Application forms obtainable from and returnable to the Secretary, Royal Northern Hospital, Holloway Road, N.7, by September 4, 1956. (7332)

ROYAL FREE HOSPITAL

REGISTRAR X-ray Department

Applications are invited for the post of Registrar to the X-ray Department at the Royal Free Hospital. The post is non-resident for one year in the first instance. Duties to commence October 1, 1956. Candidates should be registered medical practitioners of not more than ten years' standing and should hold the D.M.R.(D). Formal applications, giving details of experience, etc., together with three testimonials, should be sent to the Secretary, Royal Free Hospital, Gray's Inn Road, W.C.1, not later than September 1, 1956. (7078)

THE UNITED BIRMINGHAM HOSPITALS and THE BIRMINGHAM REGIONAL HOSPITAL BOARD

Applications are invited for the joint whole-time appointment of:

NON-RESIDENT REGISTRAR
in Diagnostic Radiology
(Senior Registrar Grade)

The duties will be apportioned at five sessions in the Teaching Hospital and six sessions in the Dudley Road Hospital Group, mainly at Dudley Road Hospital. Candidates must be registered medical practitioners, have had previous experience in the specialty and possess a diploma in radiology. Forms of application may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned by September 8, 1956. (7276)

RHEUMATOLOGY

THE UNITED SHEFFIELD HOSPITALS / SHEFFIELD REGIONAL HOSPITAL BOARD

Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases

REGISTRAR

required at the above Centre, which has an Out-Patient, an In-Patient and a Chemical Research Unit. A Registrar is required to assist in the study and treatment of severe rheumatic diseases. Previous experience in this field is not essential, but candidates must have an interest in research. Applications immediately, with the names of three referees, to the Chief Administrative Officer, The United Sheffield Hospitals, West Street, Sheffield, 1, from whom further details may be obtained. (7277)

SURGERY

AMENDED ADVERTISEMENT

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

SURGICAL REGISTRAR, Central Middlesex Hospital, Park Royal, N.W.10. Vacancy date should read "December 1." Full details shown on Page 34, August 18 issue. (7072)

SOUTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD

Applications are invited for an appointment as part-time

CONSULTANT GENERAL SURGEON

for 9 notional half days a week in the Canterbury, Isle of Thanet and St. Augustine's groups of hospitals. The successful candidate will be required to reside in the Canterbury area. Candidates must have had wide experience in General Surgery, and be Fellows of a Royal College of Surgeons. Applicants may visit the hospitals concerned. Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of three referees, to: The Secretary, Advisory Appointments Committee, South-East Metropolitan Regional Hospital Board, 11, Portland Place, W.1, not later than September 15, 1956. (7159)

SOUTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD

Applications are invited for an appointment as part-time

CONSULTANT GENERAL SURGEON

for 9 notional half days a week in the South-East Kent group of hospitals. The successful candidate will be required to reside in the area. General Surgical experience is essential. Special training and experience in Urology would be an asset for candidates, who must be Fellows of a Royal College of Surgeons. The appointment will be in accordance with the Terms and Conditions of Service of Hospital Medical and Dental Staff (England and Wales). Candidates may visit the hospitals concerned. Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and war service, together with the names and addresses of three referees, to: The Secretary, Advisory Appointments Committee, South-East Metropolitan Regional Hospital Board, 11, Portland Place, W.1, not later than September 15, 1956. (7160)

Surgery—contd.

N.E. METROPOLITAN REGIONAL HOSPITAL BOARD

SURGICAL REGISTRAR (Resident)
Tilbury & Riverside General Hospital, Tilbury Essex

Recognized for F.R.C.S. Active Surgical Unit and busy Out-patient Department in all Specialties.

SURGICAL REGISTRAR
(Resident or Non-resident)
Bethnal Green Hospital, E.2

Recognized for F.R.C.S.

SURGICAL REGISTRAR (Non-resident)
Whipps Cross Hospital, Leytonstone, E.11

Recognized for F.R.C.S.

Appointments subject to review after one year. Application forms from Secretary, 11a, Portland Place, W.1, to be returned by September 8. (7352)

CHICHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE
(South-West Metropolitan Regional Hospital Board)

SENIOR REGISTRAR, General Surgery

Locum wanted for one month, possibly longer, chiefly Royal West Sussex Hospital. £24 per week. Non-resident. Apply Group Secretary, 174, Broyle Road, Chichester. (7171)

DUDLEY, GUEST HOSPITAL
(154 beds)

REGISTRAR GENERAL SURGERY

Experience specialty essential. Higher qualification desirable. Resident. Application forms from Group Secretary to be returned by September 3, 1956. Candidates may visit Hospital. (7209)

LEEDS REGIONAL HOSPITAL BOARD

REGISTRARS IN GENERAL SURGERY

(a) Hull Royal Infirmary (80 General Surgical beds) and other hospitals in the Hull (A) Group. Non-resident. Includes additional duties in the Casualty Department.

(b) Halifax Group. Mainly the Royal Halifax Infirmary (110 General Surgical beds). Preferably resident. Includes some duties in the Casualty Department.

Applications, stating age, qualifications and details of present and previous appointments (showing dates), together with the names and addresses of three referees, to the Secretary, Joint Registrars Committee, Park Parade, Harrogate, by September 7, 1956. (7210)

MANCHESTER REGIONAL HOSPITAL BOARD

Bury and Rossendale Hospital Management Committee

Applications are invited for
REGISTRAR IN SURGERY

at Bury General Hospital, the post falling vacant at the end of August. Post recognized for F.R.C.S. Applications, together with the names of two referees, should be sent to the undersigned.—H. Wilkinson, Group Secretary, Bury General Hospital, Bury, Lancs. (7288)

MANCHESTER REGIONAL HOSPITAL BOARD

Applications invited for the post of whole-time
RESIDENT SURGICAL REGISTRAR

to the West Manchester Hospital Management Committee with duties primarily at Park Hospital, Davyhulme, but with duties at other hospitals within the Group. Post vacant early September. 12 months' appointment subject to renewal. Form from Secretary, Park Hospital, Davyhulme. (7365)

MANCHESTER REGIONAL HOSPITAL BOARD

South Manchester H.M.C.

Applications are invited from registered medical practitioners for two posts of
RESIDENT SURGICAL OFFICER
(Registrar Grade)

at the Wythenshawe Hospital. Each post will include responsibility for General Surgical beds and one post will include responsibility for Gynaecological beds. Both posts are recognized by the Royal College of Surgeons. Applications, stating age, qualifications, present post, and names of two referees, to be forwarded to the Group Secretary, Withington Hospital, within seven days of the appearance of this advertisement. (7320)

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

Whole-time non-resident
SURGICAL REGISTRAR

required at Edgware General Hospital, Edgware, Middlesex (715 beds). Post vacant early October. Hospital may be visited by direct appointment with Medical Director. Application forms obtainable from and returnable to Group Secretary, Edgware General Hospital, by September 4, 1956. (7367)

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

Salisbury Group Hospital Management Committee
Regional Plastic and Oral Surgery Centre, Odstock Hospital, Salisbury, Wilts

Applications are invited for the post of
SURGICAL REGISTRAR

Candidates should have had wide surgical experience and the possession of a higher surgical degree will be an advantage. Post vacant November 16, 1956. Application forms may be obtained from, and must be returned to, the Group Secretary, Odstock Hospital, Salisbury, by September 6, 1956. (7175)

THE UNITED BIRMINGHAM HOSPITALS

Queen Elizabeth Hospital

Applications are invited for the post of
SURGICAL REGISTRAR (Registrar grade)

This post is designed to give experience in Neurosurgery and Plastic Surgery and would be suitable for trainees in General Surgery, Orthopaedic and other branches of Surgery. The appointment is tenable for six months in the first instance with the possibility of re-appointment for a further period of time. The successful candidate may be required to be resident. Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned to him by September 8, 1956. (7366)

CROYDON GROUP HOSPITAL MANAGEMENT COMMITTEE

Norwood Hospital

CLINICAL ASSISTANT—General Surgery

1 Session weekly at £175 per annum. Detailed applications in writing, with names of two referees, to George A. Paines, Group Secretary, Croydon Hospital Management Committee, General Hospital, London Road, Croydon, within 7 days of the publication of this advertisement. (7211)

MANOR HOUSE HOSPITAL
Golders Green, N.W.11
(exempted from National Health Service)

RESIDENT SURGICAL OFFICER (Male)

Required. Salary £745 per annum, less £130 per annum for emoluments. Six months' appointment, renewable. Applications, stating age, nationality, qualifications, and Surgical or "Orthopaedic experience, with copies of three recent testimonials, to: The Secretary, Mr. W. F. Pendrill. (7278)

ST. CHARLES' HOSPITAL
(581 beds)
Ladbroke Grove, W.10

Applications are invited to fill the undermentioned post:

SENIOR HOUSE OFFICER
(Orthopaedics, Ophthalmology, Plastics, E.N.T., etc.)

Applications, stating age, qualifications, experience, etc., together with names and addresses of two referees, to be forwarded to Hospital Secretary immediately. (7235)

BANBURY, OXON, HORTON GENERAL HOSPITAL (163 beds)

SENIOR HOUSE OFFICER (Surgeon)

required September 10. Hospital recognized for F.R.C.S. Active surgical department under direction of resident Consultant. Work in general surgical wards, with special responsibility for children. Four other residents. Application, with names of two referees, to the Secretary. (6952)

BLACKBURN & DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Royal Infirmary, Blackburn (262 Acute Beds)

SENIOR HOUSE OFFICER (General Surgery)

required September 29. Recognized for F.R.C.S. Apply Secretary, H.M.C. Office, Royal Infirmary, Blackburn. (7172)

CARDIFF HOSPITAL MANAGEMENT COMMITTEE

RESIDENT SENIOR HOUSE OFFICER
(Surgical)

required at Royal Hamadryad General and Seamen's Hospital: Locum appointment if desired. Post covers 44 beds, Genito-Urinary, General Surgery and Out-patients. Department under care of Consultants from United Cardiff Hospitals. Form of application from Group Secretary, 44, Cathedral Road, Cardiff. (7176)

EPPING, ST. MARGARET'S HOSPITAL
(480 beds)

RESIDENT SENIOR HOUSE OFFICER (Surgery)

Vacant October 1, 1956. Post recognized for F.R.C.S. Busy general hospital with easy access to London. Salary on national scale, less deduction for board, lodging, etc. Applications, with copies of two testimonials, to reach the Group Secretary, Epping Group H.M.C., "Oak Cottage," The Plain, Epping, Essex, by August 31, 1956. (6853)

HOSPITAL MANAGEMENT COMMITTEE No. 9 WAKEFIELD "A" GROUP

The General Hospital, Park Lodge Lane, Wakefield (158 beds)

RESIDENT SURGICAL OFFICER (S.H.O. Grade)

required at the above hospital. Post vacant immediately. Salary and conditions of service in accordance with national recommendations. Application should be made to the Group Secretary, 113, Northgate, Wakefield. (7173)

MERTHYR & ABERDARE HOSPITAL MANAGEMENT COMMITTEE

RESIDENT SENIOR HOUSE OFFICERS
(Surgical)

St. Tydfil's Hospital, Merthyr Tydfil (376 beds)
Merthyr General Hospital, Merthyr Tydfil (120 beds)

Vacancies immediately, both posts terminate January 31, 1957. Apply with full particulars and copies of two recent testimonials, to Group Secretary, St. Tydfil's Hospital, Merthyr Tydfil. (6893)

MINEHEAD & WEST SOMERSET HOSPITAL Minehead, Somerset

Applications are invited for the post of
RESIDENT SURGICAL OFFICER (S.H.O.)

with care mainly of surgical cases under Consultant Staff. One other Senior House Officer. Six months' or one year's appointment. Vacant now. Salary £745 per annum. Furnished house available for married applicant. Applications to the Secretary, Minehead and West Somerset Hospital, Minehead, Somerset. (7307)

NEWPORT, MON., ST. WOOLOS HOSPITAL
(379 beds)

SENIOR HOUSE OFFICER

required. (Non-resident.) Post is of a senior character. Surgical Department of 46 beds consists of Consultant engaged only here. House Surgeon and this post. Recognized F.R.C.S. for 6 months. Excellent experience. Write quoting two referees to T. A. Jones, Group Secretary, 64, Cardiff Road, Newport, Mon. (6390)

NOTTINGHAM HIGHBURY HOSPITAL

SENIOR HOUSE OFFICER (Surgical)

required at the above Hospital. Good opportunity for obtaining experience in all types of general surgery. Duties to commence on or about September 16, 1956. Applications, stating age, qualifications and experience and nationality, together with copies of testimonials, to be sent to the Group Secretary, General Hospital, Nottingham. (7174)

OTLEY, YORKSHIRE, THE GENERAL HOSPITAL (172 beds)

SENIOR HOUSE SURGEON (S.H.O. grade)

in general and orthopaedic surgery required to work under full consultant staff who are members of the Teaching Staff of Leeds University. Approval for F.R.C.S. pending. Applications, stating age, nationality and experience, with names of two referees, to Group Secretary. (7253)

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE

(1) Queen Alexandra Hospital
SENIOR HOUSE SURGEON
(87 surgical beds). Vacant September 1, 1956.
(2) Royal Portsmouth Hospital
SENIOR HOUSE SURGEON
(70 surgical beds). Vacant September 19, 1956.

Applications, stating age, experience and qualifications, together with the names of two referees, should be forwarded as soon as possible to E. H. Hurst, 35, Grove Road South, Southsea (6672)

RHYMNEY AND SIRHOWY VALLEYS HOSPITAL MANAGEMENT COMMITTEE

Caerphilly District Miners Hospital, near Cardiff (226 general beds)

SENIOR HOUSE OFFICER (General Surgery)

Married quarters may be available. Apply to Group Secretary, Central Offices, Caerphilly Road, Ystrad Mynach, Hengoed, Glam. (7051)

STOURBRIDGE (near), WORDSLEY HOSPITAL
(478 beds)

SENIOR HOUSE OFFICER (Surgical)

Post vacant October, 1956. Apply Group Secretary, Guest Hospital, Dudley, Worcestershire. (6842)

SUNDERLAND, GENERAL HOSPITAL

SENIOR SURGICAL HOUSE OFFICER

required, male or female (resident). Post recognized for F.R.C.S., post vacant September 12, 1956. Apply, naming two referees, to Hospital Secretary, General Hospital, Chester Road, Sunderland. (7305)

IMPORTANT: All intending applicants should read the revised NOTICE at the top of page 28

Surgery—contd.

TORQUAY DISTRICT HOSPITAL MANAGEMENT COMMITTEE

Torbay Hospital, Torquay

RESIDENT SENIOR HOUSE OFFICER (Surgery) required early September, 1956. (Post recognized for F.R.C.S.) There is a complement of 6 Resident House Officers. Applications, stating qualifications, age, nationality, with copies of testimonials (quoting Ref. F.955/72), to the Group Secretary, Torbay Hospital, Torquay, S. Devon. (7019)

NORTH CAMBRIDGESHIRE HOSPITAL MANAGEMENT COMMITTEE

County Hospital, Doddington, March, Cambs. (116 Beds—Acute)

Applications are invited for the following posts:
RESIDENT SENIOR SURGICAL OFFICER (Post-registration)
RESIDENT SURGICAL HOUSE OFFICER (Pre-registration)

Recently constructed self-contained flat for married couple available for either post. Duties: General Surgical and Orthopaedic. Whitley Council salaries and conditions. Applications, with copies of two testimonials, to the Hospital Secretary. (7127)

ST. ALFEGE'S HOSPITAL, Greenwich, S.E.10 (373 beds)
Recognized for F.R.C.S. Examination

HOUSE SURGEON
Vacant mid-September, 1956. Six months' appointment. National salary and conditions. Applications and testimonials to Secretary, G. & D./H.M.C. above Hospital. (7082)

WANSTEAD HOSPITAL
Harmon Hill, London, E.11 (191 beds)

HOUSE SURGEON
required, post vacant September 15, 1956. Recognized for F.R.C.S. Applications, with full details, and copies of two recent testimonials, should be sent immediately to Secretary, Forest Group H.M.C., Langthorne Road, E.11. (6609)

BEXHILL, BEXHILL HOSPITAL (62 beds)

HOUSE SURGEON
resident, not pre-registration post. National scales of salary. Apply to Hospital Administrator. (7179)

BIRMINGHAM ACCIDENT HOSPITAL
Bath Row, Birmingham, 15
(215 beds and 8 House Surgeons)

HOUSE SURGEONS (resident)
Vacant September. Recognized for purpose of Casualty by R.C.S. (Eng.). Teaching programme by Consultant Staff. Appointment for 6 months, some of which may be spent, at applicant's request, in 42 bedded Medical Research Council's Burns Unit. Apply within 7 days of advertisement to Administrator, naming two referees. (7212)

HULL (A) GROUP HOSPITAL MANAGEMENT COMMITTEE

Hull Royal Infirmary (Sutton)

Applications are invited for the post of
HOUSE SURGEON
Vacant September. Recognized for F.R.C.S. National salary scale and conditions. Appointment will be for six months, terminable by one month's notice either side. Applications to the Hospital Secretary, Hull Royal Infirmary. (7360)

KENT AND CANTERBURY HOSPITAL
Canterbury (277 beds)

GENERAL SURGICAL AND ORTHOPAEDIC HOUSE SURGEON
The above post, which is recognized for the F.R.C.S. Diploma, becomes vacant in mid-September, 1956. N.H.S. salary and conditions. Applications, together with two recent testimonials, to be addressed to the Hospital Secretary at the above Hospital. (6777)

ROMFORD, ESSEX, OLDCHURCH HOSPITAL (722 beds)

RESIDENT HOUSE SURGEON
required from September 29, 1956, in the General Surgical Unit at the above hospital. Recognized for F.R.C.S. This very active General Surgical Unit of a total of 180 beds affords ample opportunities for candidates to obtain first-class tuition and experience. The candidate appointed will be attached to a unit of approximately 60 beds. Applications should be forwarded immediately to Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford. (6894)

SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE

Salisbury General Hospital

Applications are invited for the appointment of
RESIDENT HOUSE SURGEON/OBSTETRIC AND GYNAECOLOGICAL HOUSE SURGEON (recognized by R.C.O.G.)
to run consecutively in this order from November 2, 1956, for a period of six months in each post. The posts are open to pre-registration candidates. Apply, enclosing two recent references, to Group Secretary, Odstock Hospital, Salisbury. (6957)

SURBITON GENERAL HOSPITAL (72 beds)

Kingston Group Hospital Management Committee

RESIDENT JUNIOR HOUSE OFFICER (Surgical) (First, Second or Third post)
Applications are invited for the above post, which becomes vacant early September, and is recognized for pre-registration purposes. Duties include Casualty Out-patients, post provides interesting experience in surgery and medicine under visiting Consultants. Salary and conditions of service in accordance with National scales. Applications, stating age, qualifications and nationality, with copies of two testimonials, to Administrative Officer, Surbiton General Hospital, Ewell Road, Surbiton, Surrey. (7126)

NEW END HOSPITAL, London, N.W.3

Applications are invited for 2 posts of
HOUSE SURGEON (Gen. Surgery)
Vacant October 1, 1956. Preference will be given to Pre-registration candidates for one position. Application forms from Group Secretary, 46, Cholmeley Park, N.6 (ARC. 3070, Ext. 24), and returnable to the Surgeon Superintendent, New End Hospital, by September 4, 1956. (7125)

HAMPSTEAD GENERAL HOSPITAL
Haverstock Hill, N.W.3
(Royal Free Hospital Group)

Applications are invited for the pre-registration post of
HOUSE SURGEON
vacant October 1, 1956, tenable for a period of six months. Application forms may be obtained from the Secretary, to whom they should be returned, together with copies of three recent testimonials, by September 5, 1956. (Pr.7324)

BIRMINGHAM, 18, DUDLEY ROAD HOSPITAL (780 beds)

HOUSE SURGEON
required. Recognized for pre-registration and F.R.C.S. Unit of approximately 85 adult and children's General Surgical beds under control of two Consultant Surgeons. Detailed applications, with copies of three recent testimonials, to Group Secretary. (Pr.7296)

BIRMINGHAM, 9, LITTLE BROMWICH GENERAL HOSPITAL

HOUSE SURGEON (Male/Female)
Post vacant September 12, 1956. Recognized as pre-registration appointment. Apply Physician Superintendent with copies of two testimonials, or names of three referees. (Pr.6955)

BURTON-ON-TRENT, THE GENERAL HOSPITAL

HOUSE SURGEON
required at the above hospital. Post recognized for Pre-Registration purposes. Apply, Group Secretary. (Pr.6565)

CAMBRIDGE, ADDENBROOKE'S HOSPITAL

HOUSE SURGEON
for 6 months from October 3. Recognized pre-registration service. Apply, stating age, nationality, qualifications and experience (with dates) and copies of three testimonials, to Secretary by September 8. Interviews mid-September. (Pr.7180)

EDGWARE GENERAL HOSPITAL
Edgware, Middlesex

TWO RESIDENT HOUSE SURGEONS
Posts vacant October 18 and 20, 1956. Six months' appointments. Posts recognized for F.R.C.S. and pre-registration purposes. Applications, stating age, qualifications, experience, and enclosing copies of up to three recent testimonials, to Medical Director of Hospital by September 1, 1956. (Pr.7099)

HUNTINGDON COUNTY HOSPITAL

Applications are invited for the post of
HOUSE OFFICER (Surgical)
now vacant. Post recognized for pre-registration purposes. Apply with full particulars, and names of two referees, to Secretary, County Hospital, Huntingdon. (Pr.7289)

LEEDS, 14, SEACROFT HOSPITAL

HOUSE OFFICER
for Children's Surgical and E.N.T. Wards. Recognized pre-registration post. Applications to Chief Administrative Officer. (Pr.7347)

KIDDERMINSTER & DISTRICT GENERAL HOSPITAL (112 beds)

Applications are invited for the pre-registration post of
HOUSE SURGEON
at the above hospital. Post vacant from August 28. Applications, with the names of three referees, to the Hospital Secretary. (Pr.6895)

NORTHAMPTON GENERAL HOSPITAL (482 beds)
Vacancy October 1, 1956, for
HOUSE OFFICER General Surgery
Recognized for F.R.C.S. and for pre-registration. Six months' appointment in first instance. Applications as soon as possible to S. C. Hill, Superintendent. (Pr.7182)

STOCKPORT AND BUXTON H.M.C.

Stockport Infirmary (163 beds)

Applications are invited for the post of
HOUSE OFFICER
(General Surgery and Ophthalmology)
vacant September 24, 1956. This post is approved for Pre-registration purposes and recognized for the F.R.C.S. and D.O.M.S. Applications, stating age, qualifications and experience, together with copies of two testimonials, to be addressed to the Secretary, Stockport and Buxton H.M.C., 59B, Shaw Heath, Stockport. (Pr.7020)

TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE

North Ormesby Hospital (180 beds), Middlesbrough

Applications are invited for the appointment of
HOUSE OFFICER (Surgical)
to Surgical Team No. 2
at the above-named Hospital. The appointment is recognized for the F.R.C.S. and also for pre-registration service under the Medical Act, 1950. Applications, stating full details, and giving two names for reference, should be addressed to the Hospital Secretary. (Pr.6958)

WEST BROMWICH AND DISTRICT GENERAL HOSPITAL (144 beds)

HOUSE SURGEON
Vacant October 1, 1956. Pre-registration. Applications, with three recent testimonials, to Group Secretary, West Bromwich and District H.M.C., Edward Street, West Bromwich. (Pr.7385)

THORACIC SURGERY

BROMPTON HOSPITAL, S.W.3

Applications invited for the post of
RESIDENT SURGICAL OFFICER
(Post graded as Senior House Officer or Registrar, according to qualifications and experience), for which there are two vacancies, for six months from November 1, 1956, with eligibility for re-appointment. Candidates must have held a resident hospital appointment. Applications, stating age, qualifications (with dates), nationality and appointments held, together with copies of testimonials, by September 8, 1956, to Kenneth A. F. Miles, House Governor. (7298)

NORTH MIDDLESEX HOSPITAL and Annexes, Edmonton, N.18

REGISTRAR in Thoracic Surgery (Non-resident)
Offers experience in all types of cardiac, oesophageal, tuberculous and non-tuberculous thoracic surgery. Appointment subject to review after one year. Application forms from Secretary, N.E. Metropolitan Regional Hospital Board, 11a, Portland Place, W.1, to be returned by September 8. (7353)

SHEFFIELD REGIONAL HOSPITAL BOARD

City General Hospital, Sheffield (652 beds)
(Recognized for Final Fellowship Examination)

WHOLE-TIME RESIDENT REGISTRAR (Thoracic Surgery)
required. Appointment for one year in first instance. General Hospital with Regional Department of Cardiology. Thoracic Surgical Unit deals with T.B. and Non-T.B. cases. Previous thoracic surgical experience desirable. Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood Road, Sheffield, by September 3, giving age, nationality, qualifications, present and previous appointments (with dates), naming three referees. (7183)

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD

SURGICAL REGISTRAR
required for the Thoracic Unit (80 Surgical Beds) at the Southampton Chest Hospital. Candidates should possess higher qualifications and have had previous experience of Thoracic Surgery. The Hospital may be visited, if desired, by prior arrangement. Application forms may be obtained from the undersigned to whom they should be returned not later than Wednesday, September 5, 1956.—Frank Jeminus, Group Secretary, Southampton Group Hospital Management Committee, Buffar Street, Southampton. (7311)

Thoracic Surgery—(contd.)

BRISTOL, COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE

SENIOR HOUSE OFFICER

required in the Thoracic Surgery Department, which is the Regional Thoracic Surgery Centre (120 beds) for the South-West. Applications, with full particulars, should be addressed to the Group Secretary, Frenchay Hospital, Bristol, quoting "Thoracic." (7372)

UNITED OXFORD HOSPITALS

Applications are invited for the post of **HOUSE SURGEON in the Thoracic Surgery Unit** at the Churchill Hospital, to commence as early as possible until January 31, 1957. Applications, stating age, qualifications and experience, together with names of two referees, to: Administrative Assistant, Radcliffe Infirmary, Oxford, as soon as possible. (7184)

UROLOGY

PRESTON AND CHORLEY HOSPITAL MANAGEMENT COMMITTEE

Preston Royal Infirmary (400 beds)

UROLOGICAL REGISTRAR

Specialist department. F.R.C.S. preferable. One of two registrar posts. Resident or non-resident. Vacant September 1. Application forms obtainable from Group Secretary, Royal Infirmary, Preston, Lancs. (7213)

IMPORTANT: All intending applicants should read the revised NOTICE at the top of page 28

PUBLIC HEALTH

ANGLESEY COUNTY COUNCIL

Applications invited from Registered Medical Practitioners to act as

LOCUM TENENS MEDICAL OFFICER

for a period of 9 to 12 months, salary at the rate of £1,576 5s. per annum. National Conditions of Service, travelling allowances, etc., will apply. Duties will include acting as Medical Officer of Health for the Borough of Beaumaris, the Urban Districts of Llangefni and Menai Bridge and the Rural District of Aethwy and as Assistant County Medical Officer and School Medical Officer. Applications, giving names of two persons to whom reference may be made, to Clerk, County Council, Shire Hall, Llangefni, by not later than September 1, 1956. (7214)

BOROUGH OF HOVE
SENIOR ASSISTANT MEDICAL OFFICER
EAST SUSSEX COUNTY COUNCIL
SCHOOL MEDICAL OFFICER

Applications are invited for the above permanent appointments from male registered medical practitioners possessing the D.P.H. The combined salary scale is £1,155 per annum, rising by three annual increments of £50 and five of £55 to £1,580 per annum. Account will be taken of previous experience in fixing the commencing salary. Car allowances are paid. The duties include work in connection with public health, infectious diseases and school medical services. Further particulars and application form may be obtained from the undersigned to whom applications should be sent so as to arrive not later than Monday, September 10, 1956.—John E. Stevens, Town Clerk. Town Hall, Hove, 3. (7308)

NOTTINGHAMSHIRE COUNTY COUNCIL
HUCKNALL URBAN DISTRICT COUNCIL
Mixed Appointment

Applications are invited from registered medical practitioners for the mixed whole-time appointment of

ASSISTANT COUNTY MEDICAL OFFICER AND MEDICAL OFFICER OF HEALTH

to the Hucknall Urban District. Applicants must have had at least three years' professional experience since qualifying, be experienced in the duties of Medical Officer of Health, School Medical Officer and the Care of Mothers and Young Children, and possess a Diploma in Public Health. Salaries are in accordance with the recommendations of the Medical Whitley Council for Public Health Medical Officers holding mixed appointments, namely (a) As Assistant County Medical Officer (32/44ths) £954 10s. 11d. by £43 15s. to £1,173 5s. 11d. (On scale £1,200 by £55 to £1,475 plus loading in accordance with Spens Formula.) (b) As Medical Officer of Health (12/44ths) £501 16s. 4d. by £15 to £561 16s. 4d. (On scale £1,740 by £55 to £1,960 plus 12/44ths of £100.) Application forms and conditions of appointment are obtainable from my office and applications should reach me by September 8, 1956. Canvassing disqualifies.—A. R. Davis, Clerk of the County Council, Shire Hall, Nottingham. (6897)

ESSEX COUNTY COUNCIL

ASSISTANT COUNTY MEDICAL OFFICERS OF HEALTH

Applications invited from male registered medical practitioners for above appointments in (a) Romford Health Area; (b) South Essex Health Area (Grays, West Thurrock, Purfleet districts). Preference given to candidates experienced in School Medical and Maternity and Child Welfare duties and possessing Diploma in Child Health and/or Certificate or Diploma in Public Health. Salary scale £1,050 by £50 to £1,200 by £55 to £1,475. Application form from County Medical Officer of Health, County Hall, Chelmsford, returnable by September 3, 1956. Canvassing disqualifies. (7128)

STAFFORDSHIRE COUNTY COUNCIL

APPOINTMENT OF ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER—SOUTH STAFFS AREA

Applications are invited from fully qualified medical practitioners and those holding the Diploma of Public Health will be given preference. The candidate appointed will undertake clinical work in the School Health and Child Welfare Services under the direction of the County Medical Officer of Health, and will be required to perform such other duties as may from time to time be prescribed. The salary scale is £1,050 by £50 to £1,200 by £55 to £1,475, and increments may be given for previous similar service. The appointment will be terminable by three months' notice in writing on either side and subject to the provisions of the appropriate Superannuation Acts and Regulations, in which connection the selected candidate must pass a medical examination and submit his or her birth certificate. Forms of application may be obtained from the County Medical Officer, County Buildings, Stafford, to whom they should be returned when completed not later than by September 4, 1956.—T. H. Evans, Clerk of the County Council, County Buildings, Stafford. (6990)

STATES OF GUERNSEY

MEDICAL OFFICER OF HEALTH

Applications are invited for the above post from registered medical practitioners. Possession of D.P.H. essential. Salary scale £1,800 per annum rising by four annual increments of £55 each to £2,020 per annum. The post is pensionable subject to the provisions of a non-contributory Staff Pension Scheme and, unless he is unable to qualify thereunder, the successful candidate will be subject to the Rules and Regulations governing a Contingency Fund to provide pensions to widows and orphans of the male members of the salaried staff. Particulars may be obtained from the Secretary, States Appointments Board, Royal Court House, Guernsey. Applications, stating age, sex, qualifications and giving details of experience, with names of three referees, to be sent to The President, States Appointments Board, Royal Court House, Guernsey, before September 15, 1956. (7369)

OVERSEA (Vacant)

AUSTRALIA, VICTORIA, PROVINCIAL CITY. Partner required. Protestant with higher medical qualification. Half share available, worth over £A.5,000 per annum. Full details from Medical Practices Advisory Bureau, B.M.A., Tavistock Square, W.C.1.

ENGLISH, IRISH, SCOTTISH OR WELSH Doctor (male) required, Pusan, Korea. General Medical qualifications. Salary £1,080 to £1,250 depending on experience, plus board and accommodation. One to two year contract. Apply Foreign Relief Secretary, Save the Children Fund, 12, Upper Belgrave Street, S.W.1. Tel.: Sloane 9171. (6432)

FOR SALE, NEW ZEALAND, SUBURBAN General Practice with city consulting work. Four-bedroom house. Income £6,000 p.a.—Box 1180, B.M.J.

WANTED: PHYSICIAN AND SURGEON FOR a Manitoba town and surrounding municipalities of approximately 3,000 people. Private practice. Well-equipped small hospital. Modern residence for rent available. Duties to commence as soon as possible. Please give particulars of qualifications and experience.—Apply by Air Mail to Secretary-Treasurer, Elkhorn Medical Nursing Unit, Elkhorn, Manitoba. (7052)

CATHOLIC MISSION HOSPITALS. VACANCIES in East and West Africa and India.—Apply Secretary, Damien Society, 47, Fitzwilliam Square, Dublin. (7130)

MEDICAL OFFICER REQUIRED BY FALKLAND Islands Dependencies Air Survey for tour of 6 months' service in Antarctic base. To leave U.K. in September, 1956. Salary £625 a year. Free passages, quarters, mending and canteen stores. Liberal leave on full salary. Candidates must possess qualifications registrable in the U.K. Write to the Crown Agents, 4, Millbank, London, S.W.1. State age, name in block letters, full qualifications and experience and quote M3/43443/BG. (7375)

A 350 BED HOSPITAL INVITES APPLICATIONS for Rotating Internships for a one year period. Honorarium $50.00 per month plus board, room and uniforms. Ideal for one year's training prior to establishing a practice in this province. Apply, stating qualifications, to (Mrs.) V. Burgoyne, R.N., Assistant Superintendent, Misericordia General Hospital, Winnipeg 1, Manitoba.

CITY OF PORT ELIZABETH
Vacancies—Health Department

ASSISTANT TUBERCULOSIS OFFICERS

Applications are invited from registered medical practitioners for two vacant positions of Assistant Tuberculosis Officers in Grade £1,020 by £60 to £1,380 per annum. The commencing salary will be commensurate with qualifications and experience. In addition to the salary a cost of living allowance, at present £234 per annum, will be payable if the appointees are married males. No cost of living allowance will be paid to single persons. A transport allowance, at present at the rate of £15 13s. 10d. per month, is payable. Applications should state qualifications, earliest date duty can be assumed, whether applicant is in receipt of a pension, and experience and be accompanied by not more than three recent testimonials. Applications must be submitted immediately to Davis & Soper Ltd., 52 & 54, St. Mary Axe, London, E.C.3. (7376)

GOVERNMENT OF BRITISH GUIANA

SURGEON

required for surgical, obstetrical and gynaecological work principally at the Public Hospital, Georgetown, including the instruction of junior Medical Officers and Nurses. He will assist the Senior Surgeons under the direction of the Director of Medical Services.

Appointment on permanent basis with pension (non-contributory) 1/600th of final pensionable emoluments for each completed month of service; or on contract for three years' resident service with gratuity (taxable) of 22½% of salary for each three months' service. Candidates in National Health Service may leave but retain their superannuation rights during their service abroad (up to 6 years) and receive a gratuity (taxable) of 20% of their salary on leaving overseas employment.

Salary £1,600 a year plus non-pensionable allowance of £250 a year in lieu of consultation fees. Free unfurnished quarters or an allowance of £100 a year in lieu. Generous home leave. Free passages on appointment for officer, wife and children under 16 years, not exceeding 5 persons in all. Assisted passages for officer and wife on leave.

Candidates must hold medical qualifications registrable in United Kingdom and F.R.C.S. and have been actively engaged in general surgery during past three years.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/30/02). (7373)

GOVERNMENT OF TRINIDAD

Applications invited from doctors with qualifications registrable in United Kingdom for following posts in Trinidad. Applicants should have three years' post-registration experience and hold the Diploma in Public Health or equivalent qualification.

(a) Public Health Department
MEDICAL OFFICER, Grade B

for work usually required of Medical Officers of Health including Public Health administration, environmental sanitation, school health, maternity and child welfare services, communicable disease control, housing, etc., and the implementation of provisions of the Ordinance and Laws relating to public health.

(b) Venereal Disease Division
MEDICAL OFFICER, Grade B

to undertake and supervise diagnostic and treatment measures in various Venereal Disease and Yaws treatment centres; to supervise the work of Junior Medical Officers, teach control and treatment measures to junior medical and nursing staff and co-operate with Public Health Officers in effecting such control. Appointment on permanent basis with pension (non-contributory), or on short term agreement. Candidate in National Health Service may leave but retain his superannuation rights (up to six years) and receive a gratuity (taxable) of 20% of his aggregate salary on completion of engagement. Salary scale B.W.I. $6,720 to B.W.I. $7,200 (£1,400 to £1,500) per annum. Government quarters if available at low rental, or an allowance in lieu. Free passages on appointment for officer and family not exceeding 5 persons in all, on leave subject to maximum of 3 adult fares. Income tax at local rates. Generous home leave. Tour of service is 3½ years. Educational facilities are available. Application forms from the Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/30/014). (7374)

WANTED, INTERNS FOR JULY, 1957. SALARY $100 monthly with full maintenance. 12 months' rotating service. Teaching programme. Write, Thomas J. Quigley, M.D., St. Vincent's Hospital, Staten Island 10, New York, N.Y.

Oversea (Vacant)—contd.

GOLD COAST LOCAL CIVIL SERVICE

Applications are invited for the following posts in the Ministry of Health, Gold Coast.

RADIOLOGIST

to take charge of Hospital X-ray departments and train junior staff as X-ray attendants. Candidates must possess D.M.R.D.

PATHOLOGIST

to carry out routine duties of Clinical Pathologists including haematology, bacteriology, histopathology and biochemistry. May be required to perform post mortem examinations and other duties in connection with forensic medicine. Candidates must have had at least 2 years' full-time approved laboratory experience.

Appointment is to Gold Coast Local Civil Service and may be

(a) Contract for two tours of duty of 18 to 24 months with gratuity (taxable) of £12 10s. for each completed month of service.

(b) Three years' probation for permanent and pensionable employment. Pension (non-contributory) at rate of 1/600th of final pensionable emoluments for each completed month of service; or

(c) Doctors in the National Health Service may leave the N.H.S. but retain their superannuation rights while in the Gold Coast (up to six years) and receive a gratuity (taxable) of 20% of their Gold Coast salary.

Salary under (a) from £1,330 to £2,310 a year and under (b) and (c) £1,055 to £1,850 a year, starting point being determined by qualifications and experience. Temporary addition of £29 15s. a year also payable.

Quarters at rental not exceeding £150 a year. Income Tax at local rates. Free passages for officer, wife, and up to three children under 13 years of age. Annual local leave permissible and generous home leave granted after each tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/13/010). (7262)

GOLD COAST LOCAL CIVIL SERVICE
Ministry of Health

SPECIALIST PHYSICIAN

required to take charge of special medical wards in large hospital and to give opinion on cases referred by medical officers and private practitioners. Candidates should hold Membership of one of Royal Colleges of Physicians and have had four years' full-time experience in work of this speciality. Appointment would be to Gold Coast Civil Service on contract for two tours of duty of from 18 to 24 months each in the first instance with gratuity on satisfactory completion of service. Basic salary scale would be £2,400 to £2,700 a year. Gratuity (taxable) of £12 10s. for each completed month of service. Candidate in National Health Service may leave N.H.S. but retain superannuation rights (up to a maximum stay of 6 years). Salary in this case would be in the scale £1,900 to £2,200 a year, and gratuity 20% of aggregate of salary. Temporary addition of £29 15s. a year also payable. Starting point in both salary scales determined according to qualifications and experience. Quarters when available at rental not exceeding £150; income tax at local rates; free passages for officer, wife and up to 3 children under 13 years of age. Generous home leave. Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/13/017). (7261)

GOVERNMENT OF BRITISH GUIANA

MEDICAL OFFICERS

required for general duties.

Appointment on permanent basis with pension (non-contributory) 1/600th of final pensionable emoluments for each completed month of service; or on contract for 3 years' resident service with gratuity (taxable) of 22½% of salary for each three months' service. Candidates in the National Health Service may leave but retain their Superannuation rights during service abroad (up to six years) and receive gratuity (taxable) of 20% of aggregate salary on leaving overseas service.

Salary scale £950 to £1,450 a year. Starting salary according to qualifications and experience. Income tax at local rates. Free unfurnished quarters or allowance in lieu when attached to Institutions, or at rental of 10% of salary in districts where quarters are available. Generous home leave. Free passages on appointment for officer, wife and children under 18 not exceeding five persons in all. Assisted passages on leave for officer and wife.

Candidates must have qualifications registrable in the United Kingdom.

Application forms from the Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/30/01). (7259)

GOVERNMENT OF BRITISH GUIANA

OBSTETRICIAN

required for the Public Hospital, Georgetown, to be responsible for obstetrical wards and ante-natal clinics, and for a number of beds for gynaecological patients. He will be required to instruct junior Medical Officers and Nurses in Obstetrics, and perform such other duties as may be assigned by the Director of Medical Services.

Appointment on permanent basis with pension (non-contributory) 1/600th of final pensionable emoluments for each completed month of service; or on contract for 3 years' resident service with gratuity (taxable) of 22½% of salary for each three months' service. Candidates in the National Health Service may leave but retain their Superannuation rights during their service abroad (up to six years) and receive a gratuity (taxable) of 20% of the aggregate of their salary on leaving overseas employment.

Salary £1,800 a year plus non-pensionable allowance of £250 a year in lieu of consultation fees. Private practice not permitted. Free unfurnished quarters provided if available or an allowance of £100 a year in lieu. Generous home leave. Free passages on appointment for officer, wife and children under 18 years, not exceeding five persons in all. Assisted passages for officer and wife on leave. Candidates must hold medical qualifications registrable in the United Kingdom and M.R.C.O.G.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/30/021). (7260)

GOVERNMENT OF NORTHERN RHODESIA

MEDICAL OFFICER

required for Silicosis Medical Bureau of the Health Department. Duties include clinical and radiological examination of miners (European and African). Officer will be stationed at Kitwe and will work under supervision of Chairman (a Medical Specialist) of the Silicosis Medical Bureau. Kitwe is a town of considerable size with agreeable climate and many social amenities. Post offers excellent opportunity for experience in diseases of chest and research in pneumoconiosis.

Appointment can be on permanent basis with pension, or short term contract with gratuity (taxable). Candidates in National Health Service may leave N.H.S. but retain their superannuation rights (up to six years) and receive a gratuity (taxable) of 20% of aggregate of salary at end of engagement. Salary scale from £1,245 to £2,030 a year, starting salary depending upon age and experience. Pension for permanent appointment at rate of 1/600th of final pensionable emoluments for each completed month of service. Gratuity for contract appointment is £37 10s. for each completed three months of service.

Free passages are provided in both directions for officer and wife, and assisted passages for children. Housing is available and married candidate may be accompanied by family. Candidates (male only) should be between 25 and 35 years of age, possess medical qualifications registrable in the United Kingdom and have had at least twelve months' postgraduate experience. Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/3/02). (7264)

HER MAJESTY'S OVERSEA SERVICE
Medical Branch, Tanganyika

MEDICAL OFFICERS

with qualifications registrable in United Kingdom required for general duties. Officers would normally be based on a hospital but must be prepared to tour and to assist in training African staff.

Appointments can be made on permanent basis with pension (non-contributory), or on short term contract with gratuity payable on satisfactory completion of service. A doctor in National Health Service may leave the N.H.S. but retain his superannuation rights (up to limit of six years) and receive a gratuity (taxable) of 20% of his aggregate salary after engagement. Salary ranges from £1,284 to £2,115 a year, starting point determined by experience. Four extra increments given to successful candidates possessing the F.R.C.S., M.R.C.P., D.P.H., or other approved higher qualifications.

Permanent Medical Officers are eligible to be considered at any time for promotion to super-scale posts in Tanganyika and other territories in medical administration or, if they possess higher qualification and suitable experience, in specialist posts.

Quarters are generally available at rental varying from £30 to £78 a year according to size and type, and furniture at rate varying from £12 to £24 a year. Free passages in both directions for officer and wife and up to cost of one adult fare for children. Taxation at local rates. Annual local leave permissible and generous home leave granted after each tour of from 30 to 36 months. Educational facilities available.

Application forms from Director of Recruitment, Colonial Office, Great Smith Street, London, S.W.1 (quoting BCD 117/8/02). (7258)

PROGRESSIVE STATE MENTAL HOSPITAL,

4,600 beds in Virginia, expanding staff, invites applications for physicians at all levels, psychiatric experience desirable but not necessary. Salary from $4,040 (approximately £2,750). All modern methods of treatments. Opportunities for research. Good retirement plan. Apply to Brian C. Campden-Main, M.R.C.S. Send full résumé in first letter. Box 271, Petersburg, Virginia, U.S.A. (6991)

REGIONAL MEDICAL HEALTH OFFICERS REQUIRED BY THE SASKATCHEWAN DEPARTMENT OF PUBLIC HEALTH

Salary: $8,112.00 to $9,588.00 per annum. Duties: To perform professional medical and administrative work as Medical Health Officer in an organized Health Region with a population of approximately 50,000, to develop regional preventive health services and a general public health programme. Requirements: Graduation from an approved Medical School; some medical and administrative experience. Diploma or Master's Degree in Public Health desirable but not essential. Benefits: Three weeks' annual vacation with pay; three weeks' sick leave, accumulative, with pay; suitable superannuation scheme. Opportunity is available for assisted post-graduate training. For application forms contact Public Service Commission, Legislative Building, Regina, Saskatchewan, Canada. For further information write to Personnel Officer, Department of Public Health, Provincial Health Building, Regina, Saskatchewan, Canada. (7070)

THE DOCTOR'S HOSPITAL
New York, U.S.A.

Applications invited for the following posts:

(1) TWO RESIDENT HOUSE PHYSICIANS
duties to commence late October.

(2) TWO RESIDENT HOUSE SURGEONS
duties to commence January 1, 1957. The monthly salary will be $300 with free board, lodging and laundry. Selected applicants will be expected to sign a contract for one year. Return passage by boat or plane will be paid for by the Hospital. Only Post-Registration graduates of British Universities who have done their military service or are exempt from it will be considered. Applications, with copies of two recent testimonials, should be sent to Box 1463 before September 10.

UNIVERSITY OF ALBERTA HOSPITAL
Edmonton, Alberta, Canada

ASSISTANT SUPERINTENDENT (Medical)
required. Starting salary $7,800 per annum. Annual increments of $500 to $9,800. Give full particulars, name referees, and enclose photograph first letter, to A. C. McGugan, M.D., Superintendent, University of Alberta Hospital, Edmonton, Alberta, Canada. (6451)

WESTERN REGION OF NIGERIA

1. SPECIALIST OBSTETRICIANS

required for obstetrical and gynaecological duties, including out-patient, maternity, child welfare and ante-natal work in the larger provincial hospitals of the Region (which are being enlarged up to 200 beds), and to assist in training midwives. Candidates should have registrable medical qualifications and the M.R.C.O.G., with considerable experience of major surgery in their speciality, and have had at least six years' post-registration experience.

2. SPECIALIST RADIOLOGIST

required to give advice on Radiological equipment of hospitals in the Region, advise and assist medical officers in the interpretation of X-ray films, travel in the Region supervising the work of X-ray technicians and radiographers, and be responsible for the ordering and supplying of departmental X-ray stores. Candidates should possess registrable medical qualifications and the D.M.R.D. plus four years' experience in their speciality.

Appointments may be:

(a) from the National Health Service. Candidates may leave the National Health Service but retain their superannuation rights up to six years and receive a gratuity (taxable) of 20% of the aggregate of their salary.

or (b) on short term contract (one tour in first instance of 12 to 24 months' duration according to age).

Salary under (a) £2,220 a year, and (b) £2,448 and gratuity (taxable) on satisfactory completion of contract at rate of £37 10s. for each completed period of three months' service (including leave).

Officers appointed under (b) required to contribute to Widows' and Orphans' Pension Scheme.

Quarters provided at low rental. Taxes at local rates. Annual leave permissible: generous home leave granted after each tour of 18 to 24 months. Free return passages for officer, wife and children (up to 3).

Application forms from Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD 117/410/06. (7263)

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APPOINTMENTS, etc.

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POST OF CLINICAL DIRECTOR AT THE Hardon Neurological Institute. Candidates should possess some knowledge of neuropsychiatry, and be prepared to take part in research. Salary according to experience, but not less than that of a Registrar. Initial appointment for one year. Apply, Director, Stoke Lane, Stapleton, Bristol. (7328)

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Applications are invited for the full-time post of **FIRST ASSISTANT (Senior Lecturer Grade)** in the new Research Department of Anaesthetics. Applicants should be medically qualified, and should have had experience in physiological research. Starting salary will be in the range £1,250 to £1,750 according to qualifications and experience. The post is superannuable and a family allowance is payable. Applications, in writing (two copies), giving details of qualifications and experience, together with the names of two referees, should be sent to Mr. W. P. Davis, Secretary, Faculty of Anaesthetists, Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, by September 12, 1956. (7079)

UNIVERSITY OF BIRMINGHAM
Faculty of Medicine

Applications are invited for the post of **LECTURER in Experimental Pathology (Metabolic Diseases)** (Grade II—Clinical) for a period of one year in the first instance. Salary scale £700 to £1,700; F.S.S.U. and family allowances. The successful candidate will be required to take up duty not later than October 1, 1956. In addition to teaching responsibilities, the duties include investigation and supervision of patients with renal and other forms of metabolic diseases. Applications (six copies), with names of two referees, should be sent by September 1, 1956, to the Assistant Registrar, the Medical School, Birmingham, 15, from whom further particulars may be obtained.—G. L. Barnes, Secretary. The University, Birmingham, 15. (7316)

PERSONAL

HYPNOTISM. THE BRITISH JOURNAL OF MEDICAL HYPNOTISM. Quarterly, £1 1s. per annum. Orders to the publishers, 4, Victoria Terrace, Hove, 3, Sussex.

PRIVATE BARGAINS

Microscope, almost new, what offers? Klein Wetzlar, No. 13242, oil immersion.—Apply 90, Manor Drive, Ewell. Tel. E.3221.

EDUCATIONAL AND LECTURES

M.R.C.P. LONDON. Correspondence coaching course recently prepared by experienced tutors, includes help with the clinical examination.—Write, J. Arnold, 189, Regent Street, W.1.

POSTAL COACHING FOR ALL MEDICAL EXAMINATIONS. Examination successes 1940-1955: M.R.C.P.Lond., 234; F.R.C.S.Eng., Primary, 185; F.R.C.S.Eng., Final, 262; M. and D.Obst. R.C.O.G., 317; D.A., 262; D.C.H., 183; Universities and Conjoint Finals, 753. Up-to-date courses for the M.D.Lond., M.R.C.P.Edin., F.R.C.S.Edin., D.P.H., F.F.A., D.P.M. Assistance with M.D. Thesis. Prospectus, list of passes, etc., on application to G. E. Oates, M.D., M.R.C.P.(Lond.), University Examination Postal Institution, 17, Red Lion Square, London, W.C.1. 'Phone: HOLborn 6311

THE MILROY LECTURES ON STATE MEDICINE AND PUBLIC HEALTH

The Council of the Royal College of Physicians of London are prepared to receive applications for the office of

MILROY LECTURER for 1958

Applications must be addressed to the Registrar, Royal College of Physicians, Pall Mall East, S.W.1, to reach the College on or before Wednesday, September 5, 1956, and to include a short synopsis of the subject selected by the candidate. Two Lectures are to be given on a Tuesday and Thursday in February or March, 1958. A copy of Dr. Milroy's "Suggestions" on the subject of his bequest, and information as to the emoluments, may be obtained from the Registrar. (6566)

POSTGRADUATE STUDY.—Diploma in Anaesthetics; Diploma in Psychological Medicine; Diplomas in Ophthalmology; Diplomas in Radiology; Diplomas in Laryngology; Diploma in Child Health; F.R.C.S.Eng. and all Surgical Examinations. M.R.C.P.Lond. and all Medical Examinations. M.D. Thesis of all Universities; Courses for all qualifying examinations. Complete Guide to Medical Examinations sent free on application. Applicants should state in which qualification they are interested. Address, Secretary, Medical Correspondence College, 19, Welbeck St., London, W.1.

SITUATIONS VACANT

Imperial Chemical Industries Limited has a vacancy for a graduate, preferably under 30 years of age, trained in bacteriology for investigational work in problems arising out of the use of the Company's pharmaceutical products. The successful candidate, after a short period of training at Blackley, in North Manchester, will be required to work near Wilmslow, Cheshire. Applications, with full particulars, should be addressed to the Staff Manager (H), Imperial Chemical (Pharmaceuticals) Limited, Fulshaw Hall, Wilmslow, Cheshire.

Warneford and Park Hospitals Management Committee.

Park Hospital for Functional Nervous Disorders

Secretary-in-charge

required for busy Out-patient Department. The work, which requires a good educational standard, includes, and high shorthand and typewriting speeds, is varied and interesting. Salary on Whitley Council Grade C (£435 to £580). Accommodation available, if required, in modern Nurses' Home. Applications, with the names of two referees, to The Secretary, Warneford and Park H.M.C., The Warneford Hospital, Oxford. (7327)

PHARMACISTS, DIETITIANS DISPENSERS, NURSES, ETC.

VACANT

Lady Dispenser-Secretary required for pleasant rural practice, Northumberland. Qualification not essential. Furnished cottage available.—Box 1230, B.M.J.

RECEPTIONISTS, SECRETARIES, TYPISTS, HOUSEKEEPERS, ETC.

VACANT

Experienced Secretary for busy general practice partnership in small town, 40 miles West of London.—Box 1482, B.M.J.

AVAILABLE

Doctor's wife, experienced secretary, seeks part-time post, central London, rapid shorthand-typing, French.—Box 1464, B.M.J.

Applicants requiring testimonials, theses, copied or duplicated, should communicate with Manton Secretarial Service, Ltd., 98, Victoria Street, S.W.1 (Victoria 01411, who are specialists.

"Hand-picked" doctors' Secretaries, including S.R.N.—Wigmore Agency for Medical Secretaries, 67, Wigmore Street, W.1. HUNter 9881/2/3.

Thoroughly-trained Temporary or Permanent Medical Secretarial Staff may be engaged through Brook Street Bureau of Mayfair, Ltd., 99, Brook Street, W.1. MAY 8856.

Typewriting and Duplicating. First-class work. Electric typewriters. Moderate.—Sybil Rang, 21, Heath Street, N.W.3. HAM 5329/0504.

CONSULTING ROOMS, ETC.

AVAILABLE

Consulting Rooms and Suites with or without Residential accommodation; Annual: Lee Clark and Partners, Limited, 8, Wimpole Street, W.1. Langham 1095.

Harley Street District, West End address. Telephone number. Secretarial services, and part-time or occasional use of well-furnished Consulting Rooms at nominal rent.—Box 1261, B.M.J.

ACCOMMODATION

(Convalescence, Holidays, etc.)

AVAILABLE

CONSULTING/TREATMENT ROOM TO LET in professional house, Park Street, W.1. Rent only £275 per annum inclusive. Part also available if required. Apply Dudley Samuel & Harrison Ltd., 11, Bruton Street, London, W.1. Telephone: MAYfair 7111.

FURNISHED SERVICE FLATLETS WITH maid service, breakfast, own bathroom, etc., 4 miles Marble Arch. Rents from £9 10s. per week.—Mendoza & Co., 104, Baker Street, W.1. Wel. 8341

WANTED

ACCOMMODATION WANTED BY DOCTOR'S family. Cheltenham/Gloucestershire area. Available for evening surgeries/visits week.—Box 1305, B.M.J.

HOUSES AND PROPERTY FOR SALE

The possibility of opening up a practice is NOT implied by the appearance of an advertisement under this heading.

Freehold Property for Sale in the centre of Brentwood, Essex. Full details will be given upon enquiry to C. H. & Co., 8, Western Road, Romford, Essex.

HOTELS

CENTRAL WALES.—ABERNANT LAKE HOTEL, Llanwrtyd Wells. For rest, recreation, personal attention and excellent cuisine. Lovely country setting. Privately owned golf course, fishing, tennis, shooting, riding, pony trekking. Interesting brochure on application.

PENTWALL. A.A.-R.A.C. HOTEL. OVERlooking sea, safe bathing, Bar & television lounges. Baby sitter evenings. Vacancies September. Terms 8 to 9 guineas.—67, ANDREWS HOTEL, Post Isaac. Phone 246.

MOTOR CARS, HIRE, ETC.

Rolls Royce 25/30 Hooper limit saloon, excellent condition and appearance £750.—Box 1097, B.M.J.

MISCELLANEOUS

For Sale.—Complete range of E.N.T. Instruments in first class condition.—Box 1486, B.M.J.

For Sale, Transportable attachment for Watson's B.500.—Box 1484, B.M.J.

Rent free modern flat, garage, offered Doctor. Duties phones, beds, few medical. 75 miles London.—Box 1472, B.M.J.

Bronze Nameplates, send size and lettering for free proof.—Abbey Craftsmen, 98, Cumberland Street, N.W.1. EUSton 5722.

Bronze Name Plates with crown enamel lettering. Send size and lettering for estimate.—Osborne, 117, Gower Street, London, W.C.1.

Savile Row Cutters. Consult expert extramurally, direct from eminent tailors. Ellison, Lesley & Roberts, etc. Suits, overcoats, from 16 gns.—Regent Dress Co. (Second Floor), 17, Shaftesbury Avenue, Piccadilly Circus, W.1 (next Café Monico). GER 7189. Est. over 30 years.

HOMES

HEIGHAM HALL, NORWICH

Private Mental Hospital. Individual treatment. Special Geriatric Unit. Accommodation Alcholics. From 7 gns. Apply Dr. J. A. Small. Norwich 20080.

HITCHAM PLACE, BURNHAM, BUCKS
(Late Feststation, Christchurch Road, S.W.)

A Private Home for the treatment of LADIES with Mental and Nervous Disorders, Psychotherapy, Physiotherapy, etc. A large Country Mansion with 20 acres in Green Belt. Apply Dr. Madeline R. Lockwood. Resident Physician Superintendent. Tel. Burnham 624. Station: Taplow.

MIDDLETON HALL
MIDDLETON-ST.-GEORGE, CO. DURHAM
Tel.: Dinsdale 7.

Private Mental Hospital. Cases include addiction and senility. All modern treatments, including psychotherapy. Moderate fee. Apply to Resident Physician.

MEDICAL PRACTICES ADVISORY BUREAU

APPOINTMENTS INFORMATION SERVICE

Doctors seeking information about openings in the various fields of medical practice or interested in locums, assistantships or partnerships, are invited to address enquiries to the Medical Practices Advisory Bureau at

B.M.A. House, Tavistock Square, London, W.C.1. Telephone number: EUSton 5691/3.

39, Cross Street, Manchester. Telephone number: Deansgate 3691.

7, Drumsheugh Gardens, Edinburgh, 3. Telephone number: Central 7184.

134, St. Vincent Street, Glasgow, C.2. Telephone number: Central 8656.

The services of the Medical Practices Advisory Bureau are free to members of the Association

AGENTS

PERCIVAL TURNER, LTD.

MEDICAL AGENCY (Est. 75 years)

35, Maiden Lane, Strand, W.C.2. Telephone: TEMple Bar 9011. Night: Walton-on-Thames 1203.

Overseas (Vacant)—contd.

GOLD COAST LOCAL CIVIL SERVICE

Applications are invited for the following posts in the Ministry of Health, Gold Coast.

RADIOLOGIST

to take charge of Hospital X-ray departments and train junior staff as X-ray attendants. Candidates must possess D.M.R.D.

PATHOLOGIST

to carry out routine duties of Clinical Pathologists including haematology, bacteriology, histopathology and biochemistry. May be required to perform post mortem examinations and other duties in connection with forensic medicine. Candidates must have had at least 2 years' full-time approved laboratory experience.

Appointment is to Gold Coast Local Civil Service and may be

(a) Contract for two tours of duty of 18 to 24 months with gratuity (taxable) of £12 10s. for each completed month of service.

(b) Three years' probation for permanent and pensionable employment. Pension (non-contributory) at rate of 1/600th of final pensionable emoluments for each completed month of service: or

(c) Doctors in the National Health Service may leave the N.H.S. but retain their superannuation rights while in the Gold Coast (up to six years) and receive a gratuity (taxable) of 20% of their Gold Coast salary.

Salary under (a) from £1,330 to £2,310 a year and under (b) and (c) £1,055 to £1,850 a year, starting point being determined by qualifications and experience. Temporary addition of £29 15s. a year also payable.

Quarters at rental not exceeding £150 a year. Income Tax at local rates. Free passages for officer, wife, and up to three children under 13 years of age. Annual local leave permissible and generous home leave granted after each tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/13/010). (7262)

GOLD COAST LOCAL CIVIL SERVICE
Ministry of Health

SPECIALIST PHYSICIAN

required to take charge of special medical wards in large hospital and to give opinion on cases referred by medical officers and private practitioners. Candidates should hold Membership of one of Royal Colleges of Physicians and have had four years' full-time experience in work of this speciality. Appointment would be to Gold Coast Civil Service on contract for two tours of duty of from 18 to 24 months each in the first instance with gratuity on satisfactory completion of service. Basic salary scale would be £2,400 to £2,700 a year. Gratuity (taxable) of £12 10s. for each completed month of service. Candidate in National Health Service may leave N.H.S. but retain superannuation rights (up to a maximum stay of 6 years). Salary in this case would be in the scale £1,900 to £2,200 a year, and gratuity 20% of aggregate of salary. Temporary addition of £29 15s. a year also payable. Starting point in both salary scales determined according to qualifications and experience. Quarters when available at rental not exceeding £150; income tax at local rates; free passages for officer, wife and up to 3 children under 13 years of age. Generous home leave. Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/13/017). (7261)

GOVERNMENT OF BRITISH GUIANA

MEDICAL OFFICERS

required for general duties.

Appointment on permanent basis with pension (non-contributory) 1/600th of final pensionable emoluments for each completed month of service; or on contract for 3 years' resident service with gratuity (taxable) of 22½% of salary for each three months' service. Candidates in the National Health Service may leave but retain their Superannuation rights during service abroad (up to six years) and receive gratuity (taxable) of 20% of aggregate salary on leaving overseas service.

Salary scale £950 to £1,450 a year. Starting salary according to qualifications and experience. Income tax at local rates. Free unfurnished quarters or allowance in lieu when attached to Institutions, or at rental of 10% of salary in districts where quarters are available. Generous home leave. Free passages on appointment for officer, wife and children under 18 not exceeding five persons in all. Assisted passages on leave for officer and wife.

Candidates must have qualifications registrable in the United Kingdom.

Application forms from the Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/30/01). (7259)

GOVERNMENT OF BRITISH GUIANA

OBSTETRICIAN

required for the Public Hospital, Georgetown, to be responsible for obstetrical wards and ante-natal clinics, and for a number of beds for gynaecological patients. He will be required to instruct junior Medical Officers and Nurses in Obstetrics, and perform such other duties as may be assigned by the Director of Medical Services.

Appointment on permanent basis with pension (non-contributory) 1/600th of final pensionable emoluments for each completed month of service; or on contract for 3 years' resident service with gratuity (taxable) of 22½% of salary for each three months' service. Candidates in the National Health Service may leave but retain their Superannuation rights during their service abroad (up to six years) and receive a gratuity (taxable) of 20% of the aggregate of their salary on leaving overseas employment.

Salary £1,800 a year plus non-pensionable allowance of £250 a year in lieu of consultation fees. Private practice not permitted. Free unfurnished quarters provided if available or an allowance of £100 a year in lieu. Generous home leave. Free passages on appointment for officer, wife and children under 18 years, not exceeding five persons in all. Assisted passages for officer and wife on leave. Candidates must hold medical qualifications registrable in the United Kingdom and M.R.C.O.G.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/30/021). (7260)

GOVERNMENT OF NORTHERN RHODESIA

MEDICAL OFFICER

required for Silicosis Medical Bureau of the Health Department. Duties include clinical and radiological examination of miners (European and African). Officer will be stationed at Kitwe and will work under supervision of Chairman (a Medical Specialist) of the Silicosis Medical Bureau. Kitwe is a town of considerable size with agreeable climate and many social amenities. Post offers excellent opportunity for experience in diseases of chest and research in pneumoconiosis.

Appointment can be on permanent basis with pension, or short term contract with gratuity (taxable). Candidates in National Health Service may leave N.H.S. but retain their superannuation rights (up to six years) and receive a gratuity (taxable) of 20% of aggregate of salary at end of engagement. Salary scale from £1,245 to £2,030 a year, starting salary depending upon age and experience. Pension for permanent appointment at rate of 1/600th of final pensionable emoluments for each completed month of service. Gratuity for contract appointment is £37 10s. for each completed three months of service.

Free passages are provided in both directions for officer and wife, and assisted passages for children. Housing is available and married candidate may be accompanied by family. Candidates (male only) should be between 25 and 35 years of age, possess medical qualifications registrable in the United Kingdom and have had at least twelve months' postgraduate experience. Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD 117/3/02). (7264)

HER MAJESTY'S OVERSEA SERVICE
Medical Branch, Tanganyika

MEDICAL OFFICERS

with qualifications registrable in United Kingdom required for general duties. Officers would normally be based on a hospital but must be prepared to tour and to assist in training African staff.

Appointments can be made on permanent basis with pension (non-contributory), or on short term contract with gratuity payable on satisfactory completion of service. A doctor in National Health Service may leave the N.H.S. but retain his superannuation rights (up to limit of six years) and receive a gratuity (taxable) of 20% of his aggregate salary after engagement. Salary ranges from £1,284 to £2,115 a year, starting point determined by experience. Four extra increments given to successful candidates possessing the F.R.C.S., M.R.C.P., D.P.H., or other approved higher qualifications.

Permanent Medical Officers are eligible to be considered at any time for promotion to super-scale posts in Tanganyika and other territories in medical administration or, if they possess higher qualification and suitable experience, in specialist posts.

Quarters are generally available at rental varying from £30 to £78 a year according to size and type, and furniture at rate varying from £12 to £24 a year. Free passages in both directions for officer and wife and up to cost of one adult fare for children. Taxation at local rates. Annual local leave permissible and generous home leave granted after each tour of from 30 to 36 months. Educational facilities available.

Application forms from Director of Recruitment, Colonial Office, Great Smith Street, London, S.W.1 (quoting BCD 117/8/02). (7258)

PROGRESSIVE STATE MENTAL HOSPITAL,

4,600 beds in Virginia, expanding staff, invites applications for physicians at all levels, psychiatric experience desirable but not necessary. Salary from $8,040 (approximately £2,750). All modern methods of treatments. Opportunities for research. Good retirement plan. Apply to Brian C. Campden-Main, M.R.C.S. Send full résumé in first letter. Box 271, Petersburg, Virginia, U.S.A. (6991)

REGIONAL MEDICAL HEALTH OFFICERS REQUIRED BY THE SASKATCHEWAN DEPARTMENT OF PUBLIC HEALTH

Salary: $8,112.00 to $9,588.00 per annum. Duties: To perform professional medical and administrative work as Medical Health Officer in an organized Health Region with a population of approximately 50,000, to develop regional preventive health services and a general public health programme. Requirements: Graduation from an approved Medical School; some medical and administrative experience. Diploma or Master's Degree in Public Health desirable but not essential. Benefits: Three weeks' annual vacation with pay; three weeks' sick leave, accumulative, with pay; suitable superannuation scheme. Opportunity is available for assisted post-graduate training. For application forms contact Public Service Commission, Legislative Building, Regina, Saskatchewan, Canada. For further information write to Personnel Officer, Department of Public Health, Provincial Health Building, Regina, Saskatchewan, Canada. (7070)

THE DOCTOR'S HOSPITAL
New York, U.S.A.

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duties to commence late October.

(2) TWO RESIDENT HOUSE SURGEONS
duties to commence January 1, 1957. The monthly salary will be $300 with free board, lodging and laundry. Selected applicants will be expected to sign a contract for one year. Return passage by boat or plane will be paid for by the Hospital. Only Post-Registration graduates of British Universities who have done their military service or are exempt from it will be considered. Applications, with copies of two recent testimonials, should be sent to Box 1463 before September 10.

UNIVERSITY OF ALBERTA HOSPITAL
Edmonton, Alberta, Canada

ASSISTANT SUPERINTENDENT (Medical)
required. Starting salary $7,800 per annum. Annual increments of $500 to $9,800. Give full particulars, name referees, and enclose photograph first letter, to A. C. McGugan, M.D., Superintendent, University of Alberta Hospital, Edmonton, Alberta, Canada. (6451)

WESTERN REGION OF NIGERIA

1. SPECIALIST OBSTETRICIANS

required for obstetrical and gynaecological duties, including out-patient, maternity, child welfare and ante-natal work in the larger provincial hospitals of the Region (which are being enlarged up to 200 beds), and to assist in training midwives. Candidates should have registrable medical qualifications and the M.R.C.O.G., with considerable experience of major surgery in their speciality, and have had at least six years' post-registration experience.

2. SPECIALIST RADIOLOGIST

required to give advice on Radiological equipment of hospitals in the Region, advise and assist medical officers in the interpretation of X-ray films, travel in the Region supervising the work of X-ray technicians and radiographers, and be responsible for the ordering and supplying of departmental X-ray stores. Candidates should possess registrable medical qualifications and the D.M.R.D. plus four years' experience in their speciality.

Appointments may be:

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or (b) on short term contract (one tour in first instance of 12 to 24 months' duration according to age).

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Officers appointed under (b) required to contribute to Widows' and Orphans' Pension Scheme.

Quarters provided at low rental. Taxes at local rates. Annual leave permissible: generous home leave granted after each tour of 18 to 24 months. Free return passages for officer, wife and children (up to 3).

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UNIVERSITY AND RESEARCH

APPOINTMENTS, etc.

APPLICATIONS ARE INVITED FROM Medical or Science graduates for the Boots Research Fellowship in Microbiology. Salary range £800 to £1,000 per annum with superannuation under the F.S.S.U. Some experience in Tissue Culture and Virology is desirable. Applications, stating age, qualifications and previous experience, together with the names of three persons to whom reference may be made, should be addressed to the Secretary not later than Saturday, September 8, 1956, The Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, Paddington, W.2. (7280)

POST OF CLINICAL DIRECTOR AT THE Burden Neurological Institute. Candidates should possess some knowledge of neuropsychiatry, and be prepared to take part in research. Salary according to experience, but not less than that of a Registrar. Initial appointment for one year. Apply, Director, Stoke Lane, Stapleton, Bristol. (7328)

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Applications are invited for the full-time post of FIRST ASSISTANT (Senior Lecturer Grade) in the new Research Department of Anaesthetics. Applicants should be medically qualified, and should have had experience in physiological research. Starting salary will be in the range £1,250 to £1,750 according to qualifications and experience. The post is superannuable and a family allowance is payable. Applications, in writing (two copies), giving details of qualifications and experience, together with the names of two referees, should be sent to Mr. W. F. Davis, Secretary, Faculty of Anaesthetists, Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, by September 12, 1956. (7079)

UNIVERSITY OF BIRMINGHAM
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